The gut microbiome modulates gut-brain axis glycerophospholipid metabolism in a region-specific manner in a non-human primate model of depression

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SUPPLEMENTAL MATERIALS

Supplemental Methods

Animal information

The animal experiments were performed as described previously[1-3]. Briefly, healthy and depression-like *M. fascicularis* animals were maintained at the Zhongke Experimental Animal Co., Ltd. (hereinafter "the company"), Suzhou, P.R.C. The company imported macaques from Guangdong and Vietnam in 1990, and provided them standard breeding and domestication conditions, including sufficient nutrition, daily cleanings and regular veterinary care. Macaques were reared in standard enclosures; each enclosure contains 16 to 24 macaques, 2 of which are male.

The protocol for selecting animals displaying naturally-occurring depression-like behaviors was as previously described [1]. Briefly, we surveyed the populations from 20 enclosures, and identified 6 typical depressive-like (DL) and 6 corresponding healthy control (HC) monkeys. All the 12 identified macaques were adult female, and were ruled out for disease by veterinary examination. Clinical samples are always used to uncover the association between gut microbiome and depression. Such investigations have the following shortcomings: (i) Postmortem brain tissues of patients with depression are limited, and are not suitable for uncovering how gut microbiome shapes the brain through gut-brain axis; (ii) the gut microbiome may be inevitably influenced by some confounding factors such as dietary habits, genetic, and environmental factors. By contrast, due to fixed living environment and diet, as well as highly similar genetic background, DL monkey paradigm is a useful model for uncovering the role of gut microbiome in the depression onset.

Behavioral observation

All the behavioral observations were videotaped and analyzed by NOLDUS Observer XT software (version 10.0, Noldus Information Tech Technology, Leesburg, PA). Behavioral videos were collected from January 2018 to August 2018 by 5 trained observers. To identify the DL monkeys, 6 typical DL behaviors were compared using both "free enclosures test" and "social interaction test". All the 12 identified macaques were adult female, and were ruled out for disease by veterinary examination. In every monkey cage, there were two male and 10-20 female macaques. Over time, a social hierarchy formed with one alpha and one beta male, and female *monkeys* of various rank, similarly to what happens in the wild. After a few years, some subordinate females display depression-like behaviors as they continuously suffer from the social stresses imposed by their subordinate status. For example, depression-like macaques are often the last to eat, are more socially and spatially isolated, and are actively discouraged from approaching the dominant male by the other animals[4]. As detailed elsewhere herein, these DL macaques have some characteristics, not unlike those of human depression. Thus, it serves as a highly useful new animal model for untangling the role of the microbiome in MDD.

Free enclosures test: All the DL and HC monkeys were observed within their native enclosures, and all activities were performed spontaneously without human interference. Five typical DL behaviors, including ingestion, amicable, huddle, sit alone, and locomotion, were recorded. The video records were collected for 20-30 min per shoot, with 6-7 replicates over 3 days.

Social interaction test: We designed a monkey social interaction test to evaluate communication activity in macaques based on previous behavioral models[5, 6]. Here, we used two adjacent single cages (transparent partitions) which were 70 cm long, 80 cm wide, and 90 cm high. During this experiment, a male macaque was placed in one cage, and then a female macaque was placed in another cage. The female macaque crossing the center line of her cage was defined as communication behavior. The whole process was video recorded, 30 min per shoot, 2 repeats for each macaque.

Macaque tissue preparation: Animals were deeply anesthetized and euthanized, whole brains were removed, immediately frozen in liquid nitrogen and cut in coronal

sections[7, 8]. The prefrontal cortex, hippocampus and amygdala were dissected according to a macaque brain atlas [9, 10], and stored at -80 °C until use. Peripheral tissues were dissected (liver and intestine) and blood were also collected and processed. Fecal samples were obtained from the cecum. Peripheral tissues and samples were then stored at -80 °C until use.

DNA extraction, PCR amplification, and Illumina MiSeq/HiSeq sequencing

16S rRNA gene amplicon library preparation and sequencing were performed as described previously[11, 12]. Briefly, we extracted microbial DNA from macaque fecal samples with the E.Z.N.A. soil DNA Kit (Omega Bio-tek, Norcross, GA, U.S.). Bacterial primers 338F (5'-ACTCCTACGGGAGGCAGCAG-3') and 806R (5'-GGACTACHVGGGTWTCTAAT-3') were designed to amplify the V3-V4 region of the bacterial 16S rRNA gene[13]. The PCR reaction was performed in triplicates. The amplicons were extracted using agarose gels, purified using the AxyPrep DNA Gel Extraction Kit (Axygen Biosciences, Union City, CA), and quantified using QuantiFluor™-ST (Promega, Madison, WI, USA) following the manufacturer's instructions. Then, paired-end sequencing was performed on the Illumina MiSeq platform (Illumina, San Diego, CA, USA) according to standard protocols.

The metagenomic libraries were prepared and sequenced according to our previous protocols[12, 14]. Briefly, we extracted microbial DNA from 12 macaque fecal collections using the E.Z.N.A. Stool DNA Kit (Omega Bio-tek, Norcross, GA, USA). The DNA extract was sheared using Covaris M220, aimed insert size was about 300 bp. Paired-end library was constructed using TruSeqTM DNA Sample Prep Kit (Illumina). Then, the amplicons library was paired-end sequenced on an Illumina HiSeq X platform[15].

Comparisons of Metabolite Profiles from the *M. fascicularis*

Details of the metabonomic methods were similar to our previously published protocols[12, 14]. Briefly, peripheral and brain tissue samples were prepared by homogenization, dissociation, and centrifugation, and serum samples were collected

and centrifuged twice[12]. The gas chromatography-mass spectrometry (GC/MS) three-dimensional matrices comprised of peak indices (RT-m/z pairs), sample names (observations), and normalized peak area percentages were imported into SIMCA-P 11.0 (Umetrics, Umeå, Sweden). The liquid chromatography-mass spectrometry (LC/MS) data were collected in both positive and negative ESI (electrospray ionization) modes. Discrimination of metabolites between DL and HC samples was analyzed and visualized using partial least squares discriminant analysis (PLS-DA)[16]. The differential metabolites responsible for discrimination between the two groups were identified on SIMCA, with the significance threshold of variable importance plot (VIP) > 1.0 and P-values <0.05.

Weighted gene co-expression network analysis (WGCNA)

WGCNA was used to identify key phenotype-related metagenomic and metabolic modules based on correlation patterns[17]. WGCNA was performed using R packages 'WGCNA' and 'vegan', along with official tutorials (https://horvath.genetics.ucla.edu). To describe the MGB metabolic network features comprehensively, we integrated peripheral and central metabolites into a scale-free network topology, and normalized the abundance with logarithmic conversion and robust quantile normalization. We used a 'step-by-step network construction' for metabolic network topology, adjusted network type to a 'signed hybrid' and soft thresholding power to 9 for the best topological overlap matrix, and kept other parameters as default. Considering the size of metagenomic data, we used the 'block-wise network construction' strategy and set 6 blocks. Metagenomic modules were identified with default parameters. Height cut of the metabolic and metagenomic dynamic trees were set to 0.25 consistently, and the modules with similar expression profiles were merged, then final the co-expression modules were determined.

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Supplemental Figures

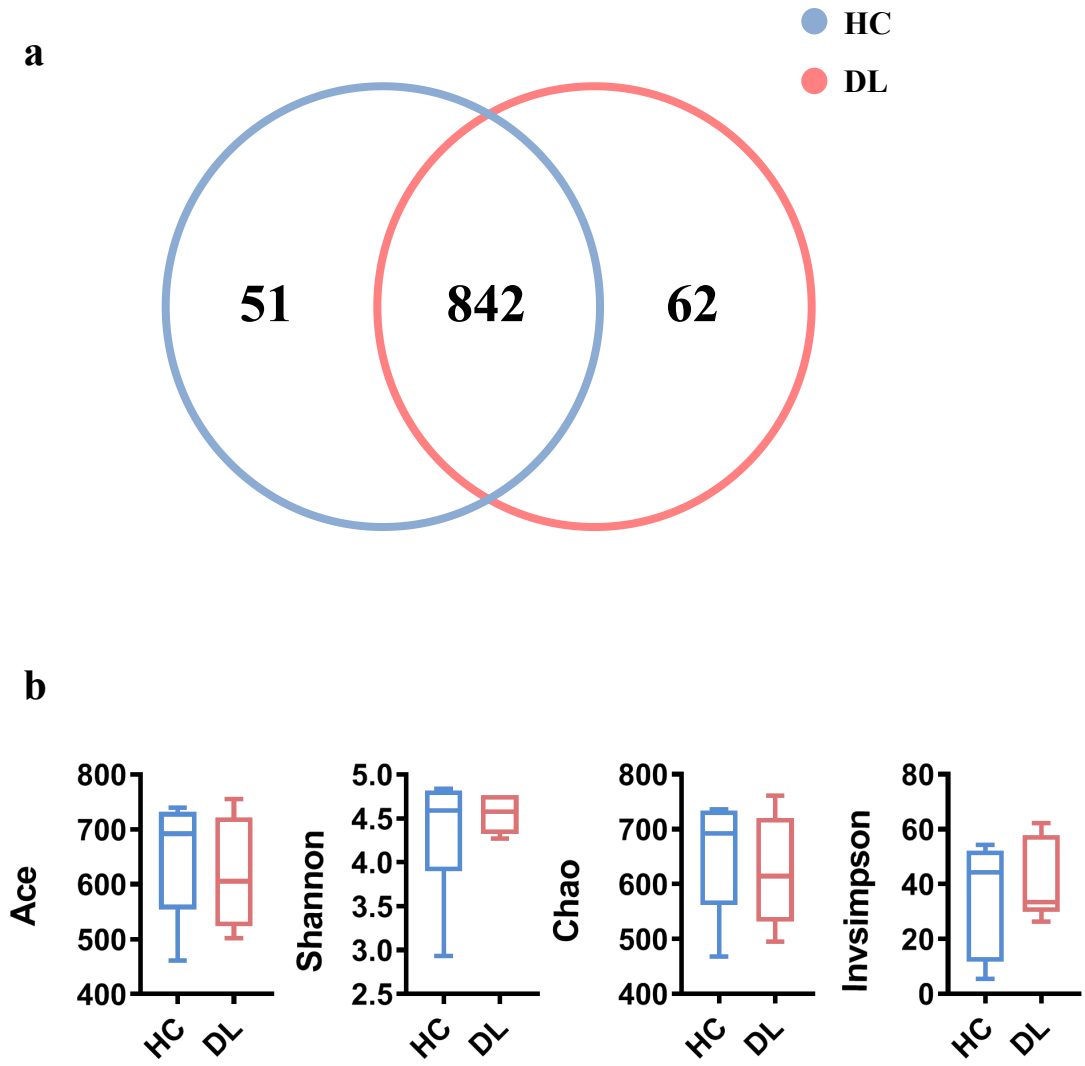
Sup Fig.1. The differences of microbial composition between depressive-like (DL) and healthy control (HC) macaques.

Sup Fig.2. Metagenomic characteristics of depressive-like (DL) M. fascicularis.

Sup Fig.3. Comparison of metabolic signatures in depressive-like (DL) and healthy control (HC) macaques.

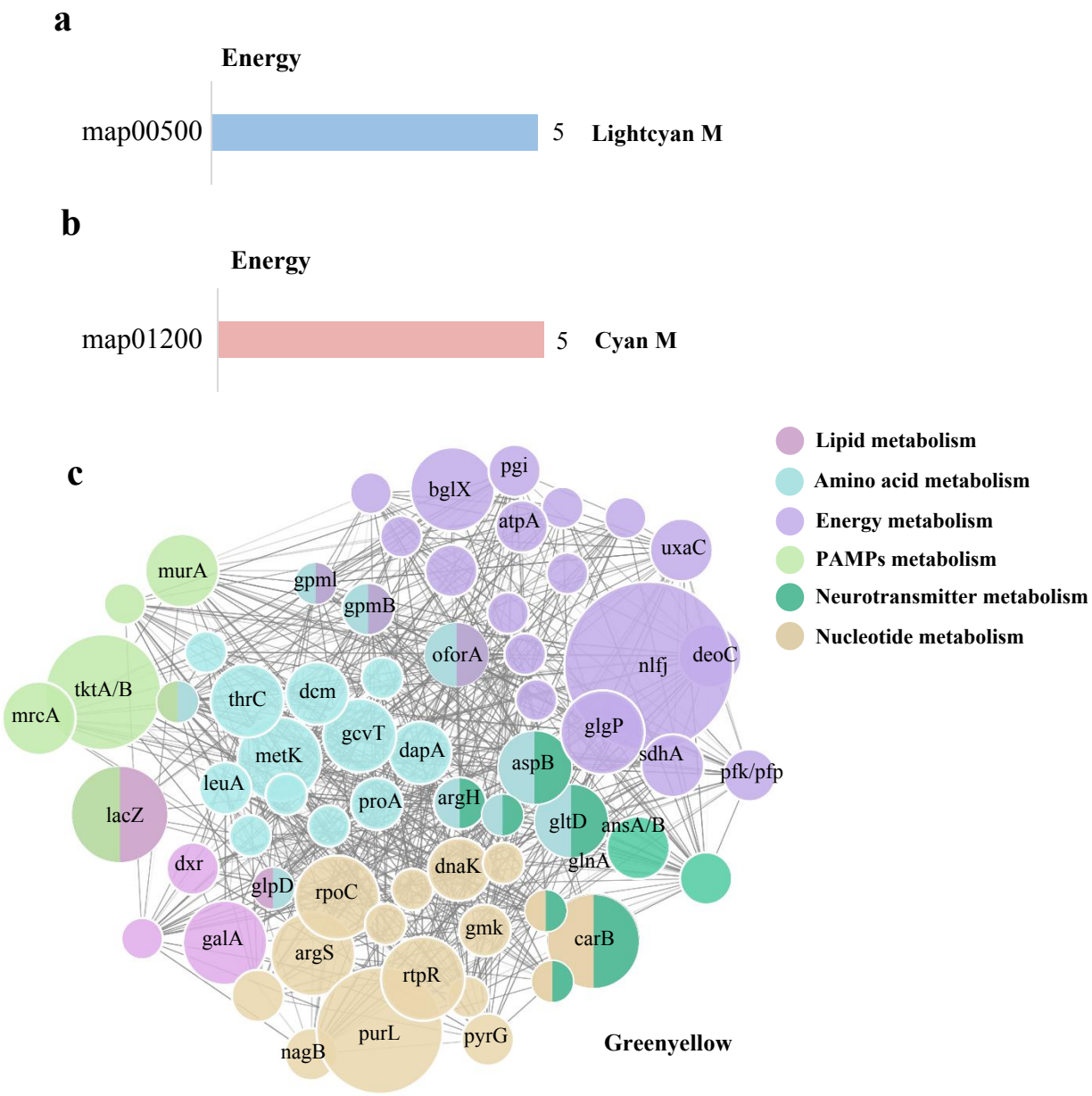
Sup Fig.4. Shared metabolites among different tissues.

Sup Fig. 1



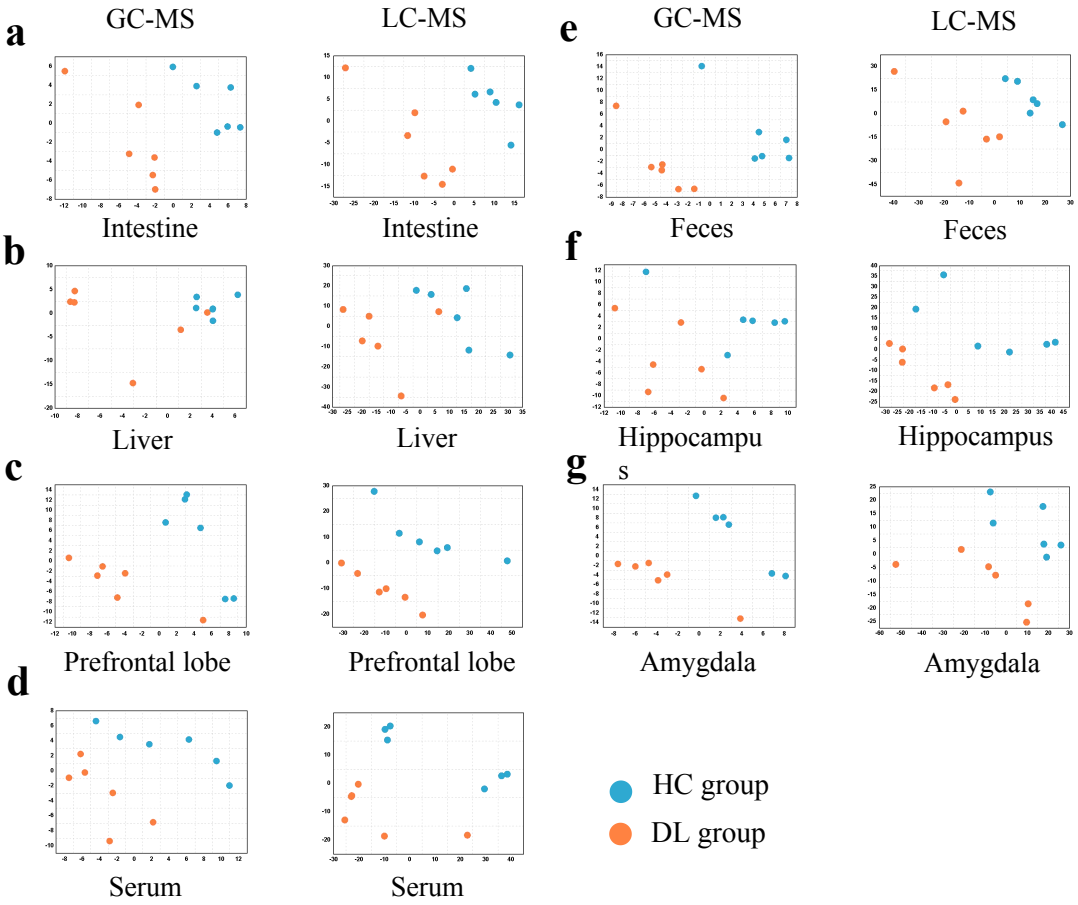
Sup Fig. 1. The differences of microbial composition between depressive-like (DL) and healthy control (HC) macaques. (a) A Venn diagram showed that 842 of 955 OTUs were common to the two groups, while 51 and 62 OTUs were unique to HCs and DLs, respectively. **(b)** α-phylogenetic diversity analysis showed no significant differences between DL and HC macaques in four indices (ACE, Chao, Shannon, and Invsimpson).

Sup Fig. 2



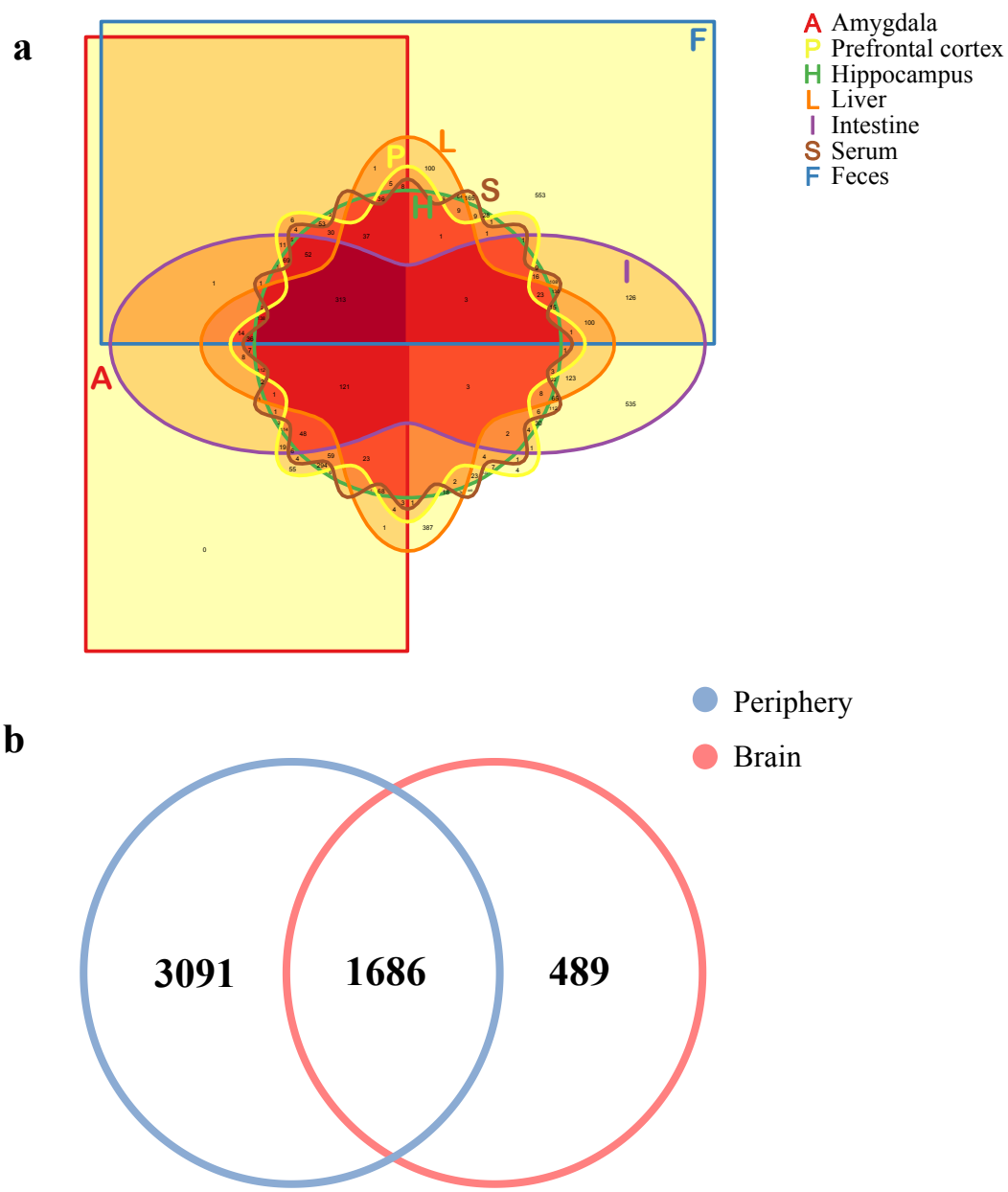
Sup Fig.2. Metagenomic characteristics of depressive-like (DL) M. fascicularis. Totally, we identified three metagenomic WGCNA modules which were significantly linked with depressive behaviors. (a-b) The two metagenomic WGCNA modules (Lightcyan M or Cyan M) were also linked with energy metabolism. (c) Microbial genes in the Greenyellow module mainly belonged to energy, neurotransmitter, nucleotide, PAMP, and lipid metabolism pathways. In the network diagram of the Greenyellow module, nodules indicating the annotated KEGG ECs, the nodule colors indicating shared bio-functional categories among the ECs, and the nodule sizes indicating the number of genes hits in each EC.

Sup Fig. 3



Sup Fig.3. Comparison of metabolic signatures in depressive-like (DL) and healthy control (HC) macaques. Comparative metabolomic analyses of samples obtained from feces, intestine, liver, serum, prefrontal lobe, hippocampus, and amygdala from DL and HC macaques were performed. Both gas chromatography and liquid mass spectrometry were used to characterize the metabolic alterations in the two groups. In these detected metabolites, the metabolic signatures of the DL group were significantly different from that of the control group across all tissues analyzed.

Sup Fig. 4



Sup Fig. 4. Shared metabolites among different tissues. (a) Venn diagram of shared metabolites among different tissues. The samples of MGB axis were diverse, these detected samples shared only a limited number of metabolites. **(b)** Venn diagram of the total number of shared metabolites between peripheral tissues (feces, serum, intestine, and liver) and brain tissues **(**amygdala, prefrontal cortex, and hippocampus).

Supplemental Tables

Sup Table 1. Depressive phenotypes of enrolled Macaca fascicularis samples

Sup Table 2. Linear discriminant analysis showing the key microbes attributing to distinguish DLs from HCs

Sup Table 3a. Gene count in metagenomic WGCNA modules.

Sup Table 3b. Detailed information of cyan module in metagenomic modules.

Sup Table 3c. Detailed information of greenyellow module in metagenomic modules

Sup Table 3d. Detailed information of lightcyan module in metagenomic modules

Sup Table 4a. Metabolomic analysis of intestinal samples obtained from DL and HC groups.

Sup Table 4b. Metabolomic analysis of serum samples obtained from DL and HC groups.

Sup Table 4c. Metabolomic analysis of hippocampus samples obtained from DL and HC groups.

Sup Table 4d. Metabolomic analysis of feces samples obtained from DL and HC groups.

Sup Table 4e. Metabolomic analysis of liver samples obtained from DL and HC groups.

Sup Table 4f. Metabolomic analysis of prefrontal cortex samples obtained from DL and HC groups.

Sup Table 4g. Metabolomic analysis of amygdala samples obtained from DL and HC groups.

Sup Table 5a. Metabolite count in metabolomic WGCNA modules.

Sup Table 5b. Detailed information of 4 metabolic modules.

[Sup Tables below]

Sup Table 1. Depressive phenotypes of enrolled Macaca fascicularis samples

Sample ID	Group	behavioral duration					
		huddle (s)	locomotion	ingestion	alone sit	amicable	communication with male
A	DL	381.0506	69.49278	89.02778	901.7811	194.0472222	24.35
B	DL	227.4022	113.5222	20.47722	1046.494	95.975	12.13
C	DL	198.825	45.4185	58.343	1009.506	138.4975	40.21
D	HC	0.555556	338.555	25.405	30.36167	173.7233333	136.67
E	HC	0	427.7263	34.79632	41.99789	190.3426316	604.86
F	HC	0	466.5658	39.27947	57.67263	147.7289474	494.51
G	DL	148.785	65.82389	32.01056	943.6622	31.975	52.17
H	DL	97.74722	52.17222	15.60611	736.9989	47.30555556	17.54
I	DL	123.1933	109.7033	27.13111	858.4689	40.34555556	22.44
J	HC	0.111111	516.9639	58.75889	5.418889	142.5838889	540.8
K	HC	1.119444	389.5806	108.1694	10.99444	83.50222222	180.17
L	HC	1.902778	367.5811	79.17167	7.237222	98.24166667	334.61

Sup Table 2. Linear discriminant analysis showing the key microbes attributing to distinguish DLs from HCs

OTU ID	Taxonomic Assignment	Relative Abundance in DL (%)		Relative Abundance in HC (%)		P value	DL Relative to HCs
		MEAN	SEM	MEAN	SEM		
OTU857	p__Cyanobacteria;c__Cyanobacteria;o__norank_c__Cyanobacteria;f__norank_c__Cyanobacteria;g__norank_c__Cyanobacteria;s__Vitis_vinifera_subsp._caucasica	0.92	0.15	0.85	0.33	0.04	UP
OTU222	p__Firmicutes;c__Erysipelotrichia;o__Erysipelotrichales;f__Erysipelotrichaceae;g__Erysipelotrichaceae_UCG-004;s__uncultured_bacterium_g__Erysipelotrichaceae_UCG-004	0.57	0.21	0.00	0.00	0.02	UP
OTU115	p__Firmicutes;c__Negativicutes;o__Selenomonadales;f__Veillonellaceae;g__Anaerovibrio;s__uncultured_bacterium_g__Anaerovibrio	5.41	1.91	1.42	0.55	0.02	UP
OTU827	p__Firmicutes;c__Negativicutes;o__Selenomonadales;f__Veillonellaceae;g__Megasphaera;s__uncultured_bacterium_g__Megasphaera	0.39	0.18	0.00	0.00	0.02	UP
OTU389	p__Firmicutes;c__Negativicutes;o__Selenomonadales;f__Veillonellaceae;g__Mitsuokella;s__uncultured_bacterium_g__Mitsuokella	2.84	1.22	0.25	0.10	0.04	UP
OTU190	p__Firmicutes;c__Negativicutes;o__Selenomonadales;f__Veillonellaceae;g__Allisonella;s__uncultured_bacterium_g__Allisonella	0.65	0.31	0.14	0.10	0.05	UP
OTU173	p__Firmicutes;c__Negativicutes;o__Selenomonadales;f__Veillonellaceae;g__Mitsuokella;s__unclassified_g__Mitsuokella	4.31	2.28	0.19	0.13	0.05	UP
OTU591	p__Firmicutes;c__Negativicutes;o__Selenomonadales;f__Acidaminococcaceae;g__Acidaminococcus;s__uncultured_bacterium_g__Acidaminococcus	2.51	1.45	0.04	0.04	0.05	UP
OTU890	p__Firmicutes;c__Clostridia;o__Clostridiales;f__Lachnospiraceae;g__Lachnospira;s__unclassified_g__Lachnospira	0.70	0.19	0.12	0.05	0.01	UP
OTU495	p__Firmicutes;c__Clostridia;o__Clostridiales;f__Lachnospiraceae;g__Lachnospira;s__uncultured_bacterium_g__Lachnospira	3.34	1.28	1.05	0.37	0.04	UP

OTU812	**p__Firmicutes;c__Clostridia;o__Clostridiales;f__Lachnospiraceae;g__Blautia;s__Ruminococcus_sp._5_1_39BFAA**	**41.35**	**7.35**	**29.86**	**6.35**	**0.04**	**UP**
OTU481	**p__Firmicutes;c__Clostridia;o__Clostridiales;f__Lachnospiraceae;g__[Eubacterium]_eligens_group;s__uncultured_bacterium_g__[Eubacterium]_eligens_group**	**11.90**	**4.29**	**3.00**	**1.06**	**0.02**	**UP**
OTU917	**p__Firmicutes;c__Clostridia;o__Clostridiales;f__Lachnospiraceae;g__Blautia;s__Blautia_obeum**	**22.35**	**3.51**	**18.29**	**4.17**	**0.02**	**UP**
OTU189	**p__Firmicutes;c__Clostridia;o__Clostridiales;f__Ruminococcaceae;g__Ruminiclostridium_9;s__uncultured_Clostridia_bacterium_g__Ruminiclostridium_9**	**0.88**	**0.22**	**0.69**	**0.28**	**0.02**	**UP**
OTU123	**p__Firmicutes;c__Clostridia;o__Clostridiales;f__Ruminococcaceae;g__Ruminococcaceae_UCG-014;s__unclassified_g__Ruminococcaceae_UCG-014**	**0.06**	**0.03**	**0.44**	**0.13**	**0.03**	**DOWN**
OTU394	**p__Firmicutes;c__Clostridia;o__Clostridiales;f__Ruminococcaceae;g__Ruminococcaceae_UCG-010;s__unclassified_g__Ruminococcaceae_UCG-010**	**0.00**	**0.00**	**0.25**	**0.09**	**0.02**	**DOWN**
OTU754	**p__Firmicutes;c__Clostridia;o__Clostridiales;f__Ruminococcaceae;g__Ruminococcaceae_UCG-014;s__unclassified_g__Ruminococcaceae_UCG-014**	**0.40**	**0.26**	**4.84**	**3.41**	**0.02**	**DOWN**
OTU669	**p__Firmicutes;c__Clostridia;o__Clostridiales;f__Ruminococcaceae;g__Ruminococcaceae_UCG-013;s__uncultured_Clostridiales_bacterium_g__Ruminococcaceae_UCG-013**	**0.10**	**0.08**	**1.01**	**0.41**	**0.05**	**DOWN**
OTU3	**p__Firmicutes;c__Clostridia;o__Clostridiales;f__Ruminococcaceae;g__Ruminococcaceae_UCG-014;s__unclassified_g__Ruminococcaceae_UCG-014**	**0.08**	**0.08**	**1.10**	**0.53**	**0.03**	**DOWN**
OTU998	**p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Streptococcaceae;g__Streptococcus;s__unclassified_g__Streptococcus**	**0.32**	**0.15**	**16.93**	**14.13**	**0.04**	**DOWN**
OTU984	**p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Streptococcaceae;g__Streptococcus;s__unclassified_g__Streptococcus**	**0.06**	**0.03**	**2.13**	**0.91**	**0.04**	**DOWN**
OTU350	**p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Carnobacteriaceae;g__Granulicatella;s__unclassified_g__Granulicatella**	**0.06**	**0.05**	**1.40**	**1.04**	**0.05**	**DOWN**
OTU660	**p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Aerococcaceae;g__Abiotrophia;s__uncultured_bacterium_g__Abiotrophia**	**0.00**	**0.00**	**0.38**	**0.30**	**0.02**	**DOWN**
OTU981	**p__Firmicutes;c__Bacilli;o__Bacillales;f__Family_XI_o__Bacillales;g__Gemella;s__unclassified_g__Gemella**	**0.13**	**0.07**	**2.11**	**0.85**	**0.04**	**DOWN**

OTU164	**p__Firmicutes;c__Clostridia;o__Clostridiales;f__Defluviitaleaceae;g__Defluviitaleaceae_UCG-011;s__unculture d_bacterium_g__Defluviitaleaceae_UCG-011**	**0.02**	**0.02**	**0.19**	**0.07**	**0.05**	**DOWN**
OTU125	**p__Firmicutes;c__Clostridia;o__Clostridiales;f__unclassified_o__Clostridiales;g__unclassified_o__Clostridiales; s__unclassified_o__Clostridiales**	**0.05**	**0.05**	**0.38**	**0.15**	**0.05**	**DOWN**
OTU651	**p__Bacteroidetes;c__Bacteroidia;o__Bacteroidales;f__Prevotellaceae;g__Prevotella_7;s__unclassified_g__Prevot ella_7**	**0.01**	**0.01**	**0.41**	**0.18**	**0.05**	**DOWN**
OTU758	**p__Proteobacteria;c__Epsilonproteobacteria;o__Campylobacterales;f__Helicobacteraceae;g__Helicobacter;s__ Helicobacter_macacae**	**0.60**	**0.28**	**12.52**	**5.17**	**<0.01**	**DOWN**

Sup Table 3a. Gene count in metagenomic WGCNA modules.

Module	n.Genes
black	18661
blue	29983
brown	23739
cyan	1465
green	22087
greenyellow	7919
grey60	1054
lightcyan	1260
lightgreen	963
magenta	9677
midnightblue	1443
pink	18508
purple	9258
red	20456
salmon	3154
tan	6494
turquoise	32198
yellow	22549

Sup Table 3b. Detailed information of cyan module in metagenomic modules.

Pathway ID	Pathway name	KO	Enzyme	Hit genes
map01212	Fatty acid metabolism	K00059	fabG	1
map01212	Fatty acid metabolism	K00645	fabD	1
map01212	Fatty acid metabolism	K01897	ACSL	3
map01212	Fatty acid metabolism	K01962	accA	1
map00061	Fatty acid biosynthesis	K00059	fabG	1
map00061	Fatty acid biosynthesis	K00645	fabD	1
map00061	Fatty acid biosynthesis	K01897	ACSL	3
map00061	Fatty acid biosynthesis	K01962	accA	1
map00561	Glycerolipid metabolism	K00864	glpK	1
map00561	Glycerolipid metabolism	K07407	E3.2.1.22B	1
map00561	Glycerolipid metabolism	K11529	gck	1
map00564	Glycerophospholipid metabolism	K00057	gpsA	3
map00564	Glycerophospholipid metabolism	K00096	araM	1
map00600	Sphingolipid metabolism	K01190	lacZ	1
map00600	Sphingolipid metabolism	K07407	E3.2.1.22B	1
map00603	Glycosphingolipid biosynthesis - globo and isoglobo series	K07407	E3.2.1.22B	1
map00071	Fatty acid degradation	K01897	ACSL	3

Sup Table 3c. Detailed information of greenyellow module in metagenomic modules

Pathway ID	Pathway name	KO	Enzyme	Hit genes
map00564	Glycerophospholipid metabolism	K00057	gpsA	3
map00564	Glycerophospholipid metabolism	K00111	glpA	5
map00564	Glycerophospholipid metabolism	K00655	plsC	4
map00564	Glycerophospholipid metabolism	K00981	E2.7.7.41	2
map00564	Glycerophospholipid metabolism	K00995	pgsA	1
map00564	Glycerophospholipid metabolism	K01126	E3.1.4.46	4
map00564	Glycerophospholipid metabolism	K01613	psd	2
map00564	Glycerophospholipid metabolism	K03735	eutB	1
map00564	Glycerophospholipid metabolism	K04019	eutA	1
map00564	Glycerophospholipid metabolism	K06131	clsA_B	4
map00564	Glycerophospholipid metabolism	K08591	plsY	4
map00561	Glycerolipid metabolism	K00005	gldA	2
map00561	Glycerolipid metabolism	K00128	ALDH	1
map00561	Glycerolipid metabolism	K00655	plsC	4
map00561	Glycerolipid metabolism	K00864	glpK	3
map00561	Glycerolipid metabolism	K00865	glxK	1
map00561	Glycerolipid metabolism	K03429	ugtP	1
map00561	Glycerolipid metabolism	K03621	plsX	3
map00561	Glycerolipid metabolism	K05878	dhaK	2
map00561	Glycerolipid metabolism	K07406	melA	1
map00561	Glycerolipid metabolism	K07407	E3.2.1.22B	9
map00561	Glycerolipid metabolism	K08591	plsY	4

map01212	**Fatty acid metabolism**	**K00059**	**fabG**	**2**
map01212	**Fatty acid metabolism**	**K00248**	**ACADS**	**2**
map01212	**Fatty acid metabolism**	**K00626**	**E2.3.1.9**	**1**
map01212	**Fatty acid metabolism**	**K00645**	**fabD**	**1**
map01212	**Fatty acid metabolism**	**K00648**	**fabH**	**1**
map01212	**Fatty acid metabolism**	**K01897**	**ACSL**	**5**
map01212	**Fatty acid metabolism**	**K01961**	**accC**	**2**
map01212	**Fatty acid metabolism**	**K01962**	**accA**	**1**
map01212	**Fatty acid metabolism**	**K02371**	**fabK**	**1**
map01212	**Fatty acid metabolism**	**K09458**	**fabF**	**1**
map01212	**Fatty acid metabolism**	**K16363**	**lpxC-fabZ**	**1**
map00061	**Fatty acid biosynthesis**	**K00059**	**fabG**	**2**
map00061	**Fatty acid biosynthesis**	**K00645**	**fabD**	**1**
map00061	**Fatty acid biosynthesis**	**K00648**	**fabH**	**1**
map00061	**Fatty acid biosynthesis**	**K01897**	**ACSL**	**5**
map00061	**Fatty acid biosynthesis**	**K01961**	**accC**	**2**
map00061	**Fatty acid biosynthesis**	**K01962**	**accA**	**1**
map00061	**Fatty acid biosynthesis**	**K02371**	**fabK**	**1**
map00061	**Fatty acid biosynthesis**	**K09458**	**fabF**	**1**
map00061	**Fatty acid biosynthesis**	**K16363**	**lpxC-fabZ**	**1**
map00071	**Fatty acid degradation**	**K00128**	**ALDH**	**1**
map00071	**Fatty acid degradation**	**K00248**	**ACADS**	**2**
map00071	**Fatty acid degradation**	**K00626**	**E2.3.1.9**	**1**
map00071	**Fatty acid degradation**	**K01897**	**ACSL**	**5**
map00071	**Fatty acid degradation**	**K04072**	**adhE**	**1**

map00603	**Glycosphingolipid biosynthesis - globo and isoglobo series**	**K07406**	**melA**	**1**
map00603	**Glycosphingolipid biosynthesis - globo and isoglobo series**	**K07407**	**E3.2.1.22B**	**9**
map00603	**Glycosphingolipid biosynthesis - globo and isoglobo series**	**K12373**	**HEXA_B**	**4**
map00600	**Sphingolipid metabolism**	**K01190**	**lacZ**	**10**
map00600	**Sphingolipid metabolism**	**K07406**	**melA**	**1**
map00600	**Sphingolipid metabolism**	**K07407**	**E3.2.1.22B**	**9**
map00604	**Glycosphingolipid biosynthesis - ganglio series**	**K12373**	**HEXA_B**	**4**

Sup Table 3d. Detailed information of lightcyan module in metagenomic modules

Pathway ID	Pathway name	KO	Enzyme	Hit genes
map01212	Fatty acid metabolism	K00645	fabD	1
map01212	Fatty acid metabolism	K00647	fabB	1
map01212	Fatty acid metabolism	K01897	ACSL	1
map01212	Fatty acid metabolism	K01963	accD	1
map00604	Glycosphingolipid biosynthesis - ganglio series	K12373	HEXA_B	1
map00603	Glycosphingolipid biosynthesis - globo and isoglobo series	K12373	HEXA_B	1
map00600	Sphingolipid metabolism	K01190	lacZ	2
map00600	Sphingolipid metabolism	K01201	GBA	1
map00564	Glycerophospholipid metabolism	K00111	glpA	2
map00564	Glycerophospholipid metabolism	K03735	eutB	1
map00564	Glycerophospholipid metabolism	K08591	plsY	1
map00564	Glycerophospholipid metabolism	K08744	CRLS	1
map00561	Glycerolipid metabolism	K00005	gldA	1
map00561	Glycerolipid metabolism	K00864	glpK	3
map00561	Glycerolipid metabolism	K00865	glxK	2
map00561	Glycerolipid metabolism	K08591	plsY	1
map00071	Fatty acid degradation	K01897	ACSL	1
map00071	Fatty acid degradation	K13953	adhP	1
map00071	Fatty acid degradation	K13954	yiaY	1
map00061	Fatty acid biosynthesis	K00645	fabD	1
map00061	Fatty acid biosynthesis	K00647	fabB	1
map00061	Fatty acid biosynthesis	K01897	ACSL	1

map00061	**Fatty acid biosynthesis**	**K01963**	**accD**	**1**

Sup Table 4a. Metabolomic analysis of intestine samples obtained from DL and HC groups.

Platform	Metabolites	Relative Abundance in DL monkeys		Relative Abundance in HC monkeys		P value	DL/CON
GC/LC	Name	MEAN	Std	MEAN	Std		UP/DOWM
LC	(23S)-1alpha-hydroxy-25,27-didehydrovitamin D3 26,23-lactone	5.904490452	0.199372131	5.411252267	0.268862172	0.004772	Up
LC	11,15-Dimethyltritriacontane	6.59744949	1.574253093	4.036752403	2.239617509	0.044918	Up
LC	11-Methylhexacosane	7.587834515	0.676961132	6.812572045	0.232353028	0.036917	Up
LC	12,13-Dimethyl-5,14-dioxabicyclo[9.2.1]-tetradeca-1(13),11-dien-4-one	4.240793305	0.572560035	3.006258341	1.098525013	0.034784	Up
LC	12beta,16beta,20R-trihydroxy-cholest-1,4-dien-3-one	5.362588435	0.319694933	6.32338101	0.513756359	0.003013	Down
LC	13,14-dihydroxy-docosanoic acid	3.672523791	0.529281869	2.630852501	0.638035545	0.011682	Up
LC	13-keto-9Z,11E,15Z-octadecatrienoic acid	8.53048377	0.063578454	8.689904171	0.132477606	0.024003	Down
LC	13-tetradecen-2,4-diyn-1-ol	3.629154908	0.134152766	3.831333211	0.172588041	0.046925	Down
LC	14-methyl-8-hexadecen-1-ol	9.209180614	0.628632429	7.67084665	1.311959852	0.026943	Up
LC	14-O-(beta-D-glucopyranosyl)-7S,14R-dihydroxy-7,9,13,17-tetramethyl-2E,4E,8E,10E,12E,16E-octadecahexaenoic acid	6.063761354	1.096804679	5.010033564	0.3607128	0.04938	Up
LC	15-HETE-DA	3.672195384	1.15257187	1.297910793	1.8519658	0.023648	Up
LC	16,16-dimethyl-PGE1	-.661807767	4.019602302	5.316566095	3.305637985	0.018354	Down
LC	19,20-DiHDPA	1.503773268	0.379303877	0.668291382	0.741220932	0.0338	Up
LC	1-Methylhistamine	3.234384262	0.591254757	2.482279629	0.417126914	0.029061	Up
LC	1-Octacosene	5.391334045	0.076898989	5.542399721	0.146752685	0.049554	Down
LC	2,6,8,12-Tetramethyl-2,4-tridecadien-1-ol	7.379141192	0.301655338	7.977766815	0.331812282	0.008432	Down
LC	24:3(15Z,18Z,21Z)	5.585404551	0.198208717	5.188635418	0.351737045	0.036859	Up
LC	24-Nor-5beta-chol-22-ene-3alpha,7alpha,12alpha-triol	3.236001149	0.506306741	2.612069442	0.333689993	0.030367	Up

LC	26:5(11Z,14Z,17Z,20Z,23Z)	5.072771047	0.279791738	4.355016072	0.61445458	0.026309	Up
LC	2-aminomuconic acid semialdehyde	4.051580745	0.302461538	3.476910709	0.444429923	0.025666	Up
LC	2-deoxy-20-hydroxy-5alpha-ecdysone 3-acetate	4.915529757	0.398416721	4.334080687	0.433330119	0.036091	Up
LC	2-keto-n-caprylic acid	4.751938713	0.100147448	4.914458732	0.141595569	0.044605	Down
LC	2-methyl-2-dodecenoic acid	3.190446171	0.94481006	2.07843577	0.63736693	0.037959	Up
LC	3beta-Hydroxy-5alpha,6alpha-epoxy-9-oxo-9,10-seco-5-cholest-7-en-11-al	7.008682441	0.339969318	7.747437823	0.375414939	0.005071	Down
LC	3'-Deoxydryopteric acid	4.334217519	1.29038249	5.908306227	1.084877803	0.045235	Down
LC	3-hydroxy-suberic acid	4.606828427	0.075469365	4.819687279	0.150457215	0.011297	Down
LC	3-keto-n-caprylic acid	5.063599858	0.224310968	4.634069769	0.245350352	0.010074	Up
LC	3'-O-methylbatatasin III	2.871265753	0.793971086	0.366674798	1.894980785	0.021408	Up
LC	3S-squalene-2,3-epoxide	2.412583393	1.472072614	0.66528964	1.180610305	0.04672	Up
LC	3Z,6Z,9Z,12Z,15Z-Tricosapentaene	8.511694326	0.206674135	8.103308029	0.338641743	0.030311	Up
LC	3Z,6Z-Eicosadiene	2.659168658	0.226332152	2.131197802	0.354453341	0.011737	Up
LC	5,7,3',5'-Tetrahydroxy-3,6,8,4'-tetramethoxyflavone	5.295420829	0.091598441	5.510105495	0.195144575	0.034885	Down
LC	5,7,4'-Trihydroxyflavanone 7-sulfate	4.812505575	1.588595916	2.144629358	1.835745108	0.022628	Up
LC	5alpha,9alpha-epidioxy-cholest-7-en-3beta,6alpha-diol	2.684617875	0.52810527	1.382652727	0.988913357	0.017408	Up
LC	5alpha-Cholestane-3alpha,7alpha,16alpha,26-tetrol	4.791916026	1.792363664	2.523765892	1.440329507	0.036295	Up
LC	5-Carboxypyranocyanidin 3-O-beta-glucopyranoside	2.419576444	0.522430789	1.673650698	0.522522002	0.032946	Up
LC	5-HEPE	6.345456932	0.647094948	5.322230598	0.766433987	0.031517	Up
LC	5S,9S-Dimethyloctadecane	2.225265989	1.58110549	3.954725527	0.80424074	0.03808	Down
LC	7-Acetoxy-7,8-dihydroiodovulone I	1.88120702	0.097749362	1.617826208	0.266200663	0.046176	Up
LC	7-Ethyl-3,11-dimethyl-1,3Z,6E,10-tridecatetraene	6.82587076	0.138535214	6.477844672	0.331653073	0.039156	Up
LC	7-Ketocholesterol	2.256457282	0.86893143	0.429114876	0.337826844	0.000722	Up
LC	7-oxo-8-amino-nonanoic acid	2.666743946	0.238389166	2.029429612	0.237558019	0.000924	Up
LC	8beta-Hydroxy-3-longipinen-5-one	4.38277528	0.086232881	4.550467048	0.150028413	0.039029	Down

LC	9,12,13-TriHOME	8.281236524	0.41665488	8.787039008	0.349428351	0.04591	Down
LC	Adenosine monophosphate	7.207803715	0.29380523	6.638832958	0.307834739	0.008358	Up
LC	Allopregnanolone	7.995290758	0.883864375	6.937422964	0.591331062	0.035048	Up
LC	Alpha-ketoisovaleric acid	1.5984443	0.438030065	2.308372791	0.567910435	0.035778	Down
LC	Artelastochromene	4.407467008	0.221878735	4.03087023	0.280965434	0.027574	Up
LC	Caffeine	6.867536125	0.071214404	7.03217085	0.162187603	0.046047	Down
LC	Carnosine	2.235503763	0.500599007	3.037808249	0.456690844	0.015828	Down
LC	Cer(d18:0/25:0)	2.762248672	0.169012138	3.040148948	0.243059947	0.044303	Down
LC	Chamazulene	4.579301071	0.62561933	2.849552077	1.537460135	0.028735	Up
LC	Cholesterol sulfate	3.502299711	0.233424278	2.89776056	0.534186371	0.029355	Up
LC	Coumesterol	4.076099133	0.72096701	3.023865567	0.590581318	0.019939	Up
LC	CPA(18:1(9Z))	5.773928023	0.624161517	5.036171925	0.389407357	0.038238	Up
LC	Cytosine	3.689952389	1.071203393	2.59572297	0.447961512	0.043624	Up
LC	Dehydrodolineone	6.51379096	1.088096341	5.237038788	0.833854912	0.045682	Up
LC	Dehydrodolineone	2.839305524	1.264539894	0.91802498	0.688370837	0.008449	Up
LC	DG(22:5(4Z,7Z,10Z,13Z,16Z)/24:1(15Z)/0:0)	1.397536251	1.403820954	4.125713109	1.331613801	0.006188	Down
LC	diamino-pimelic acid	2.324260255	0.486995692	1.44801414	0.667322286	0.026578	Up
LC	Dimethyl sulfone	8.750602289	0.071786286	8.917746577	0.144207247	0.029283	Down
LC	D-Sedoheptulose 7-phosphate	5.840439636	0.598461486	5.181395399	0.33900981	0.040846	Up
LC	GlcCer(d16:1/23:0)	6.56718589	0.072923658	6.73421822	0.124167464	0.017509	Down
LC	Guanosine monophosphate	7.164726738	0.248152008	6.321821065	0.643322184	0.022134	Up
LC	Homocysteine thiolactone	5.212490627	0.134801111	4.982292606	0.189675901	0.035866	Up
LC	Homovanillic acid	5.162158689	0.095449862	5.342647037	0.17018182	0.046905	Down
LC	Hydrocinnamic acid	3.02989436	0.483048672	1.955896307	0.820515114	0.020028	Up
LC	Hydroxyphthioceranic acid (C31)	3.457439462	0.732040077	1.745301229	0.7607908	0.002634	Up

LC	Hydroxyphthioceranic acid (C42)	6.993381494	0.633068916	6.170825312	0.612113648	0.045165	Up
LC	Hypericin	5.270154473	0.779837106	4.011307699	0.745965622	0.017035	Up
LC	Ibuprofen	5.640556944	0.805445909	4.264664021	1.175477813	0.039603	Up
LC	Isorhamnetin 3-(6''-galloylglucoside)	7.15023542	0.631967942	6.050994772	0.646808451	0.013866	Up
LC	Iso-Valeraldehyde	3.633548463	0.087920082	3.828562009	0.122015844	0.009882	Down
LC	Leukotriene B4	7.29711009	0.622369706	6.260658835	0.681200816	0.020427	Up
LC	Leukotriene B4	5.858217602	0.824317515	4.683075793	0.915340804	0.041565	Up
LC	Linoleic acid	3.827477397	0.881684849	2.522332759	0.764400066	0.020845	Up
LC	L-Malic acid	6.557983489	0.48301801	5.996777648	0.296970215	0.03579	Up
LC	L-Phenylalanine	5.813652306	0.283728512	5.500451644	0.028035093	0.042408	Up
LC	L-Proline	2.725336744	0.074556584	2.535836417	0.150492173	0.019998	Up
LC	Luteolin 7-glucuronosyl-(1->2)-glucuronide-4'-glucuronide	0.911592256	1.476548654	3.006171502	1.00086713	0.016491	Down
LC	LysoPC(16:1(9Z))	9.753547912	0.858623372	8.707731875	0.546329736	0.030535	Up
LC	LysoPC(18:1(9Z))	11.13911874	0.512709161	10.47513983	0.184721265	0.013704	Up
LC	LysoPC(18:4(6Z,9Z,12Z,15Z))	-0.044734514	1.896894473	2.068105948	1.291910957	0.047771	Down
LC	LysoPC(20:0)	9.584077457	0.54196421	8.870856342	0.408852161	0.02773	Up
LC	LysoPC(22:1(13Z))	8.129247887	0.229186445	7.662899416	0.442004299	0.044685	Up
LC	LysoPC(22:4(7Z,10Z,13Z,16Z))	8.121714363	0.600100825	7.430995432	0.459206161	0.049084	Up
LC	makisterone B	3.861896129	1.462841555	2.02121897	1.324610097	0.045422	Up
LC	Malvidin 3-glucoside-5-(6''-malonylglucoside)	5.170880629	0.399137247	4.618453183	0.184078604	0.011669	Up
LC	Menthol	4.999474319	0.082339776	5.200318856	0.152129509	0.017428	Down
LC	methyl 8-[2-(2-formyl-vinyl)-3-hydroxy-5-oxo-cyclopentyl]-octanoate	10.91468484	0.06159747	11.07948025	0.151605398	0.033289	Down
LC	methyl 8-[2-(2-formyl-vinyl)-3-hydroxy-5-oxo-cyclopentyl]-octanoate	2.464923621	2.766800028	-1.293253783	1.842279394	0.019807	Up
LC	Minabeolide-1	4.696276787	0.502833628	3.947171841	0.445650918	0.021159	Up
LC	N,N-(2,2-dihydroxy-ethyl) arachidonoyl amine	6.159703179	2.96122807	2.674869198	0.834067794	0.033463	Up

LC	Naringenin 7-O-(2'',6''-di-O-alpha-rhamnopyranosyl)-beta-glucopyranoside	5.114924299	0.248624044	4.118481339	1.027339389	0.043569	Up
LC	N-linolenoyl-glutamine	2.817702434	1.139122643	1.091964317	1.382360589	0.039958	Up
LC	N-stearoyl GABA	4.630501304	0.091321658	4.73975222	0.061579695	0.035473	Down
LC	Oleic acid	8.913110766	0.377274185	8.53195136	0.171182072	0.047887	Up
LC	PA(18:1(11Z)/18:1(11Z))	1.700933213	0.60848396	2.545250027	0.309544468	0.01269	Down
LC	PA(18:1(9Z)/0:0)	6.767592884	0.614248489	6.07370043	0.409859143	0.044124	Up
LC	PA(18:1(9Z)/0:0)	7.609212153	0.502484605	6.858527764	0.418641011	0.018428	Up
LC	PA(19:1(9Z)/0:0)	10.437441	0.70355187	9.400334741	0.377595079	0.009794	Up
LC	PA(O-16:0/14:0)	2.995100966	0.423094461	2.413972589	0.449462454	0.0438	Up
LC	PA(P-16:0/15:1(9Z))	4.312130585	1.36869825	1.027635384	1.404002856	0.002134	Up
LC	PC(13:0/0:0)	5.011193504	0.851298322	3.972951994	0.687524626	0.042475	Up
LC	PC(15:1(9Z)/0:0)	7.706333215	0.808586436	6.533097575	0.553272024	0.014958	Up
LC	PC(16:0/2:0)	5.656047628	0.806150522	4.658275427	0.639316891	0.038916	Up
LC	PC(17:1(10Z)/0:0)	11.11790377	0.367640973	10.6663781	0.193317266	0.023788	Up
LC	PC(17:1(10Z)/0:0)	9.860910461	0.822663603	8.846490758	0.692472099	0.043449	Up
LC	PC(18:0/2:0)	5.843399989	0.257431866	5.457306607	0.187394996	0.014043	Up
LC	PC(18:1(9Z)/4:0)	5.074767301	0.236632405	4.225422915	0.525811157	0.004783	Up
LC	PC(19:1(9Z)/0:0)	5.546513929	0.329969897	5.015277202	0.377253005	0.02666	Up
LC	PC(19:1(9Z)/0:0)	8.740431268	0.390754988	8.116342332	0.411669644	0.022571	Up
LC	PC(19:3(10Z,13Z,16Z)/0:0)	3.334503968	0.377109502	2.721473998	0.463312604	0.030721	Up
LC	PC(19:3(10Z,13Z,16Z)/0:0)	2.710052598	0.479181956	2.055255295	0.480980093	0.03979	Up
LC	PC(O-11:1(10E)/2:0)	5.952879374	0.986863613	4.853270491	0.41427672	0.030566	Up
LC	PC(O-12:0/O-2:0)	5.2925044	0.813656307	4.278579039	0.655210521	0.038784	Up
LC	PC(O-15:0/0:0)	7.841826148	0.328710231	7.354732199	0.276480681	0.019525	Up

LC	PC(O-16:0/0:0)	9.694982938	0.32525391	9.201833538	0.283319992	0.01878	Up
LC	PC(O-16:0/0:0)	12.77993226	0.514533612	12.03114571	0.411907296	0.019357	Up
LC	PC(O-16:0/O-18:1(9Z))	5.756639453	0.089716297	5.883350735	0.069355498	0.020938	Down
LC	PC(O-16:0/O-2:0)	13.6304405	0.714143359	12.61850363	0.637243776	0.02696	Up
LC	PC(O-17:0/0:0)	7.660668652	0.528540502	6.989454431	0.491176312	0.04589	Up
LC	PC(O-18:0/14:0)	4.512286866	0.332593296	3.935365603	0.181876917	0.003924	Up
LC	PC(O-18:0/O-2:1(1E))	8.462858664	0.523702164	7.742040329	0.466178839	0.030478	Up
LC	PC(O-6:0/O-6:0)	1.718084728	1.026199281	-0.212002445	0.851268512	0.005305	Up
LC	PE(14:0/15:0)	8.324720736	1.249098174	6.905326109	0.414417896	0.037923	Up
LC	PE(14:0/18:2(9Z,12Z))	9.613163069	0.40155377	9.13121413	0.244031551	0.030788	Up
LC	PE(14:0/18:3(9Z,12Z,15Z))	7.581143109	0.45352715	8.511161438	0.673559345	0.01862	Down
LC	PE(14:1(9Z)/24:0)	6.984311564	0.077906994	7.138271715	0.128812689	0.031171	Down
LC	PE(18:1(11Z)/18:1(11Z))	4.840495249	0.398567757	5.295875335	0.294848297	0.048187	Down
LC	PE(20:1(11Z)/0:0)	7.19876021	0.814809412	6.15407121	0.59634059	0.029651	Up
LC	PE(22:4(7Z,10Z,13Z,16Z)/0:0)	7.4820353	0.516195435	6.778159052	0.466753376	0.032684	Up
LC	PE(O-18:0/O-18:0)	5.829849556	0.644216265	4.977731363	0.654892081	0.046403	Up
LC	PE(O-20:0/0:0)	5.566836065	1.107386276	4.059773258	1.002487502	0.03303	Up
LC	Peonidin	5.961280488	0.587786854	5.094088454	0.249198522	0.007654	Up
LC	PG(20:2(11Z,14Z)/22:4(7Z,10Z,13Z,16Z))	5.794865558	0.050312837	5.977192705	0.159067802	0.023214	Down
LC	PG(20:4(5Z,8Z,11Z,14Z)/0:0)	6.578891492	0.284129304	6.242714181	0.221370077	0.045304	Up
LC	PG(22:4(7Z,10Z,13Z,16Z)/0:0)	5.263688454	0.204535735	4.602770423	0.353329593	0.002663	Up
LC	PGF2alpha-11-acetate	7.314001584	0.061267522	7.486128214	0.14039983	0.020395	Down
LC	PGF2alpha-EA(d4)	4.598103152	0.059469045	4.79171732	0.148890328	0.022834	Down
LC	PGH2-EA	3.64672526	1.417934001	0.827007932	2.034933593	0.019292	Up
LC	PI(20:4(5Z,8Z,11Z,14Z)/16:1(9Z))	1.132935224	0.624215545	1.848677913	0.323340783	0.031776	Down

LC	PI(O-18:0/0:0)	6.755432336	0.787552955	5.785835552	0.674388703	0.044966	Up
LC	Pongamoside A	5.692294816	3.089450518	2.054392334	2.01009101	0.036207	Up
LC	Primflaside	3.272328763	0.242637151	2.29103925	0.338208664	0.000179	Up
LC	Prosafrinine	3.614669657	0.836841935	5.320933518	1.154269786	0.015002	Down
LC	Prostaglandin E2	8.676102067	0.058416017	8.835976443	0.148854124	0.034316	Down
LC	PS(18:1(9Z)/20:4(5Z,8Z,11Z,14Z))	1.210943848	0.712026503	2.367661819	0.622670657	0.013447	Down
LC	PS(18:4(6Z,9Z,12Z,15Z)/22:4(7Z,10Z,13Z,16Z))	7.230669265	0.315134615	6.765082405	0.278160619	0.021814	Up
LC	PS(22:1(11Z)/0:0)	4.649027547	0.421758088	3.77216461	0.787848089	0.037092	Up
LC	PS(O-18:0/0:0)	7.476824772	1.006352978	6.183861694	0.815895711	0.034575	Up
LC	Resolvin D1	9.629207567	0.082909173	9.787476784	0.129652102	0.030433	Down
LC	Sophoracoumestan A	2.690787494	1.367721447	4.373688688	1.062246149	0.038588	Down
LC	Tetrahydrocurcumin	2.047613425	0.160440268	2.264565869	0.129505795	0.027539	Down
LC	TG(12:0/12:0/18:1(9Z))[iso3]	5.060248725	0.099767684	5.254564096	0.148253778	0.023753	Down
LC	TG(16:1(9Z)/16:1(9Z)/16:1(9Z))[iso]	5.837485421	0.347523654	6.38499668	0.464212053	0.043305	Down
LC	Thonningianin B	5.050614628	1.508494273	2.786975676	1.620452427	0.031205	Up
LC	Topiramate	6.262914345	0.397114693	5.571780304	0.314948702	0.007489	Up
LC	Tricosanyl palmitoleate	6.347451929	0.960012196	5.397439533	0.377023698	0.047674	Up
LC	Uridine 5'-monophosphate	7.54492148	0.551906321	6.554861122	0.54843621	0.010932	Up
LC	Viscutin 1	3.499212667	1.207518574	1.633528341	0.829929341	0.010893	Up
LC	zymosterol intermediate 1c	3.070755992	0.490171058	1.315469151	1.464138783	0.031215	Up
GC	5-Aminovaleric Acid	0.741823048	1.9859704764	3.457201363	2.181564674	0.047807	Down
GC	Maltotriose	0.603596544	1.6064512613	2.693996766	1.42040237	0.038097	Down
GC	Digalacturonic Acid	0.428347999	0.122956678	0.937702701	0.409046164	0.027139	Down

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GC	Nicotianamine	0.460128668	0.2148305922	0.095726222	0.224642939	0.016622	Up
GC	Uracil	5.167285728	0.3827209286	4.727969076	0.250519013	0.040465	Up
GC	Succinic Acid	1.534472221	0.4414745374	1.050004108	0.265566044	0.043999	Up
GC	3-Hydroxybutyric Acid	3.676176102	0.3395768449	3.114697934	0.393166761	0.024423	Up
GC	N-Carbamoylaspartate	4.021588366	0.6862869376	2.816054342	0.633923381	0.010146	Up
GC	Fructose-1,6-Bisphosphate	2.199852785	1.8176022563	-0.329478121	1.828761353	0.037132	Up
GC	3-Phosphoglycerate	6.284178583	1.9039632987	3.65607608	2.114367606	0.047166	Up
GC	Mannonic Acid	3.180831827	2.1999167858	0.336671698	0.398173109	0.024218	Up
GC	Hydroxycarbamate	4.992195651	2.2718282700	-0.26492069	1.397413843	0.000694	Up

Sup Table 4b. Metabolomic analysis of serum samples obtained from DL and HC groups.

Platform	Metabolites	Relative Abundance in DL monkeys		Relative Abundance in HC monkeys		P value	DL/CON
GC/LC	Name	MEAN	Std	MEAN	Std		UP/DOWM
GC	Beta-Alanine	1.67202434	0.941066815	2.873660197	0.879835462	0.04542	Down
GC	Arabitol	1.99391435	0.392764884	2.90426501	0.814214103	0.033292	Down
GC	Serine	5.600799176	0.333063223	6.156001969	0.493218597	0.04539	Down
GC	1,2,4-Benzenetriol	6.694849491	2.875825416	3.197274965	0.479089102	0.030276	Up
LC	11alpha-(chloromethyl)-1alpha,25-dihydroxyvitamin D3 / 11alpha-(chloromethyl)-1alpha,25-dihydroxycholecalciferol	5.742720924	0.468601758	2.087482083	2.660668123	0.019328	Up
LC	12-bromo-octadecanoic acid	4.698500592	0.446905827	1.713817961	2.618405013	0.037848	Up
LC	18-nonadecynoic acid	5.837346203	0.401063187	6.348572506	0.178271536	0.024952	Down
LC	19-norcholestenone	6.182864222	0.272650943	6.491656371	0.18360865	0.044174	Down
LC	1alpha-hydroxy-26,27-dinorvitamin D3 25-carboxylic acid / 1alpha-hydroxy-26,27-dinorcholecalciferol 25-carboxylic acid	5.421299879	1.115397048	2.728183162	1.777160451	0.010439	Up
LC	1beta,3alpha,7alpha,12alpha-Tetrahydroxy-5beta-cholan-24-oic Acid	6.119878853	0.469309042	3.39886786	2.563907039	0.04788	Up
LC	2-hydroxy-tridecanoic acid	7.242392365	0.197570068	6.624772769	0.542812141	0.037884	Up
LC	3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid	3.668470294	4.035914272	8.631950118	3.102924388	0.038075	Down
LC	3-demethylubiquinone-9	0.149290131	1.778788396	2.264700083	0.349776146	0.017006	Down
LC	4-Acetamidobutanoic acid	-5.449217851	3.800529482	0.534445777	2.8727756	0.01171	Down
LC	5,7,3',4'-Tetrahydroxy-6,5'-di-C-prenylflavanone	4.785625916	0.383129748	5.271013378	0.330854059	0.04073	Down
LC	6-deoxyerythronolide B	4.947184397	1.44064215	3.272368707	1.067249855	0.045154	Up
LC	7alpha,12alpha,25-Trihydroxycholest-4-en-3-one	5.113758629	0.791970238	3.798635774	1.062483573	0.035395	Up

LC	**7-oxo-8-amino-nonanoic acid**	**1.384571039**	**2.302126689**	**-1.2192254**	**0.908767538**	**0.02756**	**Up**
LC	**Adonixanthin 3-glucoside**	**3.583525145**	**0.839250286**	**4.771601847**	**0.378942445**	**0.010152**	**Down**
LC	**Antiarone D**	**7.507908757**	**0.292507069**	**7.980992296**	**0.199279376**	**0.008373**	**Down**
LC	**Caloxanthin sulfate**	**5.688934214**	**1.212941365**	**2.380583203**	**3.111704606**	**0.048382**	**Up**
LC	**Fumonisin A1**	**2.37354148**	**0.377064297**	**3.028065289**	**0.260400327**	**0.005739**	**Down**
LC	**Muxiangrin III**	**5.033151811**	**0.431514134**	**5.55364172**	**0.162988386**	**0.019993**	**Down**
LC	**PA(17:2(9Z,12Z)/0:0)**	**5.328718738**	**0.276794478**	**5.893385131**	**0.22241227**	**0.002984**	**Down**
LC	**PC(16:0/P-18:1(11Z))**	**6.984127424**	**0.240804146**	**7.269870394**	**0.196413104**	**0.047985**	**Down**
LC	**PC(20:5(5Z,8Z,11Z,14Z,17Z)/24:1(15Z))**	**3.14130852**	**2.495452265**	**6.189628673**	**1.765825705**	**0.0347**	**Down**
LC	**PE(22:4(7Z,10Z,13Z,16Z)/24:1(15Z))**	**3.334897244**	**3.074699404**	**7.612341898**	**2.012684704**	**0.017217**	**Down**
LC	**PEP-16:0/18:1(11Z))**	**4.216675771**	**2.300429657**	**6.800417603**	**0.532929355**	**0.023086**	**Down**
LC	**PG(22:4(7Z,10Z,13Z,16Z)/0:0)**	**8.991625983**	**0.426868392**	**7.175564229**	**1.461431126**	**0.02738**	**Up**
LC	**Prebarbigerone**	**4.868140717**	**0.553541904**	**5.456167007**	**0.24045016**	**0.038177**	**Down**
LC	**Pseudouridine**	**4.14200029**	**0.449414191**	**3.565543442**	**0.313608292**	**0.027576**	**Up**

Sup Table 4c. Metabolomic analysis of hippocampus samples obtained from DL and HC groups.

Platform	Metabolites	Relative Abundance in DL monkeys		Relative Abundance in HC monkeys		P Value	DL/CON
GC/LC	Name	Mean	Std	Mean	Std		UP/DOWM
GC	Uridine	3.709000897	2.636887166	0.285840971	1.997540896	0.029631	Up
GC	Mannose-6-Phosphate	1.111627695	2.395602785	-2.38479803	2.205079086	0.025145	Up
GC	Glutamate	8.992221832	2.244211639	0.657753706	4.488008893	0.002256	Up
LC	(+)-Dysideapalaunic acid	3.351107021	0.417434587	2.240189622	1.028833333	0.034207	Up
LC	(6RS)-22-oxo-23,24,25,26,27-pentanorvitamin D3 6,19-sulfur dioxide adduct / (6RS)-22-oxo-23,24,25,26,27-pentanorcholecalciferol 6,19-sulfur dioxide adduct	3.995644618	0.35674736	3.104744713	0.567285632	0.008626	Up
LC	(S)-dihydrolipoic acid	4.035208433	0.418324266	3.473205951	0.308438488	0.024369	Up
LC	1-(6-[5]-ladderane-hexanyl)-2-(8-[3]-ladderane-octanyl)-sn-glycerol	5.549906876	0.547542289	4.799958805	0.504813899	0.033297	Up
LC	1-(8-[5]-ladderane-octanoyl)-2-(8-[3]-ladderane-octanyl)-sn-glycerophosphoethanolamine	13.61885487	0.330086472	13.13654831	0.245731314	0.016643	Up
LC	1'',2''-Dihydro-8-hydroxyisopentanyl-3'-methoxy-4'-O-methylalpinumisoflavone	4.442845916	0.659692603	3.07848102	1.115291115	0.027458	Up
LC	1,7Z,13Z-Pentacosatriene	6.045122542	0.423301981	5.005989866	0.525301586	0.003644	Up
LC	10E-heptadecen-8-ynoic acid	1.703034995	0.282642546	2.335045354	0.255987194	0.002288	Down
LC	10-nitro-9E-octadecenoic acid	8.574744466	0.146822632	8.291685631	0.256763711	0.041048	Up
LC	10Z,13Z,16Z-nonadecatrienenitrile	2.965309416	1.13146091	1.700463556	0.773347024	0.047316	Up
LC	11-dehydro-2,3-dinor-TXB2	7.765211991	0.391291797	7.287990823	0.338491737	0.047421	Up
LC	13S-hydroxyoctadecadienoic acid	3.373451849	0.188377037	4.555526743	0.485484961	0.001111	Down
LC	15-HETE-T	4.162408041	0.67781618	2.992160034	1.093437332	0.049997	Up
LC	16a-Hydroxyestrone	3.527802985	0.592464228	2.74217644	0.603063265	0.046074	Up

LC	17-phenyl-trinor-PGF2alpha amide	6.247742583	0.515534568	5.371646867	0.805901696	0.048744	Up
LC	1alpha,25-dihydroxy-21-nor-20-oxavitamin D3 / 1alpha,25-dihydroxy-21-nor-20-oxacholecalciferol	5.483049495	0.403234843	4.742944367	0.333156523	0.006062	Up
LC	1alpha-hydroxy-26,27-dinorvitamin D3 25-carboxylic acid / 1alpha-hydroxy-26,27-dinorcholecalciferol 25-carboxylic acid	9.332190688	0.418785902	8.694469162	0.541520482	0.045639	Up
LC	1-Methylhistidine	3.155403327	0.291976363	3.572551426	0.266803437	0.027255	Down
LC	1-tetradecanyl-2-(8-[3]-ladderane-octanyl)-sn-glycerol	4.775038658	0.570269444	3.451660381	0.814246259	0.008561	Up
LC	2',4'-Dihydroxychalcone	4.13695254	0.254182704	3.487951473	0.278154008	0.001774	Up
LC	20-carboxy-LTB4	4.473933007	0.303203731	3.673275669	0.63420676	0.019122	Up
LC	26:2(5Z,9Z)(25Me)	4.875104619	1.244498648	1.96705329	2.674852083	0.036402	Up
LC	2E,4E,8Z,10E-dodecatetraenoic acid	2.588485731	1.419679537	0.178219141	1.757971506	0.025917	Up
LC	3,5,7-Trimethyl-2E,4E,6E,8E-undecatetraene	2.143212263	0.348927738	2.776804856	0.384126278	0.013559	Down
LC	3beta,4beta,5-Trimethoxy-4'-hydroxy- (6:7)-2,2-dimethylpyranoflavan	4.178704932	0.380174289	3.506989062	0.295769945	0.006593	Up
LC	3beta,4beta,5-Trimethoxy-4'-hydroxy- (6:7)-2,2-dimethylpyranoflavan	4.570949918	0.507215013	3.454856606	0.978985029	0.03257	Up
LC	3beta-hydroxy-4beta-methyl-5alpha-cholest-7-ene-4alpha-carbaldehyde	4.357965698	0.950821818	2.545318094	1.562043302	0.03557	Up
LC	3-Buten-2-one	2.062677751	0.375669621	2.76889863	0.485908757	0.01827	Down
LC	3Z,6Z,9Z,12Z,15Z-Pentacosapentaene	4.364183768	0.741147836	3.04970027	1.013861923	0.028189	Up
LC	3Z,6Z,9Z,12Z,15Z-Tricosapentaene	10.48168772	0.526956555	9.640511675	0.749834508	0.048325	Up
LC	3Z,6Z,9Z-Octadecatriene	3.966827757	0.457248778	3.093860841	0.81486739	0.045131	Up
LC	4-hydroxy-2-oxo-Heptanedioic acid	2.832475775	0.455985327	2.166674676	0.404163466	0.02323	Up
LC	4-oxo-Retinoic acid	7.763688752	0.5464599	7.13947397	0.210645567	0.037495	Up
LC	5,7-Dimethoxy-8-prenylflavan	5.32733349	0.450740481	4.582019181	0.554278659	0.028597	Up
LC	6Z,9Z,12Z,15Z,18Z-tetracosapentaenoic acid	7.976982731	0.264950971	7.4646848	0.45280454	0.037833	Up
LC	7-Ethyl-3,11-dimethyl-1,3Z,6E,10-tridecatetraene	6.08654395	0.383048725	5.341945569	0.572583844	0.024416	Up
LC	7-Geranylformononetin	5.702794199	0.468802761	5.050346191	0.504909144	0.042804	Up

LC	7-Hydroxyflavan	2.976958673	0.104240586	3.174254788	0.169259585	0.040021	Down
LC	7-methyl-6E-hexadecenoic acid	7.545974288	0.251208733	7.000203404	0.462281225	0.029316	Up
LC	9,10-Tetracosadiene	3.092990635	0.903271023	1.397865215	0.955442446	0.010194	Up
LC	9,11alpha-epoxypregn-4-ene-3,20-dione	3.633964264	0.253465703	3.211815311	0.245980304	0.015101	Up
LC	9S-HpOTrE	8.920862814	0.269117068	8.253214335	0.378145858	0.005506	Up
LC	Acetylcysteine	2.984675326	0.437796418	0.848882005	1.767235143	0.01657	Up
LC	Ambrettolic acid	2.515677115	0.246010042	3.158380594	0.388666857	0.00652	Down
LC	Aminoacetone	3.661846491	0.164566055	3.253664788	0.409927047	0.04709	Up
LC	Bisdemalonylmonardaein	3.260708918	0.438066962	2.488046483	0.68998195	0.043086	Up
LC	Caproic acid	0.847320364	0.902295278	-0.450705125	0.485846397	0.011201	Up
LC	Cer(d18:0/24:0)	4.362398259	0.442263469	4.922130174	0.307689993	0.029122	Down
LC	CerP(d18:1/18:0)	1.889378341	0.152241019	2.629421124	0.374811064	0.003305	Down
LC	DG(18:1(11Z)/22:5(4Z,7Z,10Z,13Z,16Z)/0:0)	10.20150349	0.365609062	9.655242043	0.385897956	0.030539	Up
LC	Dimethylglycine	4.740805273	0.271399476	5.148138111	0.207084493	0.01523	Down
LC	Dimethyl-L-arginine	4.462413159	0.47765453	3.563227661	0.792599462	0.038606	Up
LC	DMG-MINO	3.86826006	0.484516801	3.157811149	0.575724918	0.043309	Up
LC	Docosatrienoic acid	9.79010906	0.373680129	9.20711819	0.503304964	0.045936	Up
LC	Dopamine 4-sulfate	4.16639919	0.667591838	2.304888654	1.757566444	0.035737	Up
LC	Eicosenoic acid	9.451419073	0.298404311	8.9733203	0.389225187	0.038101	Up
LC	fucoxanthin	4.914623317	0.752851499	4.012522992	0.386050248	0.025964	Up
LC	Gamma-Glutamylglutamine	6.930593773	0.29407329	6.311725006	0.558563618	0.037223	Up
LC	Gibberellin A36	8.89358108	0.235564542	8.393980343	0.197247235	0.002588	Up
LC	GlcCer(d18:1/18:1(9Z))	7.275212803	0.686561327	6.273007527	0.852033852	0.048714	Up
LC	Glycerophosphocholine	4.906715421	0.31443203	4.305147897	0.554609705	0.043413	Up
LC	Glyoxylic acid	3.870103428	0.254189968	3.447167399	0.202291759	0.009671	Up

LC	Gossypol	4.665598386	0.444333127	3.806102175	0.57086209	0.015557	Up
LC	Homocysteine thiolactone	5.443900456	0.167781928	5.068220957	0.371947612	0.047753	Up
LC	Inosine	8.85994354	0.407302829	9.420509978	0.342384257	0.02739	Down
LC	L-Cystine	5.645370383	0.474026944	4.13847977	1.572043575	0.048344	Up
LC	L-Glutamic acid	7.383926117	0.252964688	7.76599858	0.292037533	0.035921	Down
LC	LysoPC(18:1(9Z))	12.16002672	0.356532354	11.61899203	0.374284021	0.02819	Up
LC	LysoPC(22:5(4Z,7Z,10Z,13Z,16Z))	5.263591979	0.607019472	4.359302821	0.658840516	0.032959	Up
LC	MGDG(18:3(9Z,12Z,15Z)/16:3(7Z,10Z,13Z))	2.96069132	0.584796496	1.918779803	0.817819277	0.029441	Up
LC	Mycolipenic acid (C28)	2.186282374	0.635721812	0.597897572	1.213207991	0.01753	Up
LC	Myristic acid	5.567494276	0.294338683	5.89864833	0.127024694	0.029856	Down
LC	N-arachidonoyl GABA	6.425678249	1.069085694	4.051874677	2.342164382	0.047495	Up
LC	N-ethyl arachidonoyl amine	4.084649367	0.20871122	4.403022058	0.193469029	0.020823	Down
LC	N-Oleoylethanolamine	7.293525053	0.340397496	6.664360631	0.494352752	0.028004	Up
LC	N-palmitoyl methionine	7.731113219	0.467464215	6.531733344	1.119761361	0.035991	Up
LC	Oleic acid	14.42636378	0.115097203	14.23504431	0.143178579	0.028813	Up
LC	Oleic acid	5.912561957	0.652977433	5.051054788	0.668587712	0.047527	Up
LC	Oxidized glutathione	7.191735751	1.007749479	8.713837444	0.533891483	0.012198	Down
LC	PA(14:0/12:0)	2.63888669	0.18199736	2.938017577	0.106152232	0.005944	Down
LC	PA(14:0/18:1(9Z))	5.823209027	0.204203291	5.412455388	0.331645982	0.02726	Up
LC	PA(O-16:0/18:2(9Z,12Z))	3.229400149	0.895070251	1.307444987	1.266983523	0.012573	Up
LC	PA(P-18:0/20:5(5Z,8Z,11Z,14Z,17Z))	5.110610146	0.397797757	4.353223526	0.30261223	0.004029	Up
LC	Palmitoleic acid	9.452873205	0.245072756	8.984620721	0.387788671	0.031431	Up
LC	PC(15:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	2.606984959	0.577269111	1.397995298	1.05131111	0.033154	Up
LC	PC(15:1(9Z)/0:0)	9.514783503	0.38918225	8.860268484	0.446471102	0.022052	Up
LC	PC(20:4(5Z,8Z,11Z,14Z)/24:1(15Z))	5.289580278	1.084318495	3.71960578	1.158984846	0.035877	Up

LC	PC(O-11:1(10E)/2:0)	4.648827634	0.45631801	3.969201329	0.50827058	0.035017	Up
LC	PE(14:0/22:2(13Z,16Z))	9.819970102	0.263724557	9.419119445	0.315465698	0.038092	Up
LC	PE(15:1(9Z)/0:0)	2.351116857	0.269253137	1.759061774	0.51505364	0.031701	Up
LC	PE(18:3(9Z,12Z,15Z)/20:2(11Z,14Z))	12.56601496	0.308907063	11.96351128	0.340233532	0.009309	Up
LC	PE(20:3(8Z,11Z,14Z)/0:0)	6.896883754	0.273165586	6.33958254	0.330935081	0.009799	Up
LC	PE(22:2(13Z,16Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	8.448945833	0.298600681	7.908678356	0.510729382	0.049263	Up
LC	PE(P-18:1(11Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	12.34646632	0.378200425	11.8388559	0.369121069	0.040448	Up
LC	PG(18:1(9Z)/0:0)	8.483073385	0.836043309	9.658165514	0.5704226	0.01743	Down
LC	PG(18:1(9Z)/12:0)	8.872544375	0.202642692	8.56027919	0.220735809	0.028734	Up
LC	PI(20:0/22:2(13Z,16Z))	7.035403987	0.401449659	5.994870733	0.707581789	0.010636	Up
LC	PS(12:0/17:0)	3.063257057	0.27174965	3.425594007	0.290071093	0.049596	Down
LC	PS(17:0/20:3(8Z,11Z,14Z))	11.69924774	0.235322033	11.29992281	0.335074558	0.03803	Up
LC	Quassin	8.860379119	0.184424812	8.352867391	0.493982707	0.040115	Up
LC	Serpyllin	4.32286176	0.206919813	3.851759416	0.442699316	0.039856	Up
LC	Tephrowatsin B	7.520698832	0.320854891	6.954177425	0.293976561	0.009673	Up
LC	Tetrahydrocortisone	4.802802569	0.3645836	3.9147393	0.706453781	0.020966	Up
LC	TG(18:2(9Z,12Z)/14:0/18:3(9Z,12Z,15Z))[iso6]	7.929810705	0.244081328	8.3210506	0.335408061	0.043488	Down
LC	Vanylglycol	3.888547426	0.4106276	4.578579695	0.496110965	0.025398	Down
LC	Villosin	1.236052701	0.603642089	0.580120283	0.329783834	0.041635	Up

Sup Table 4d. Metabolomic analysis of feces samples obtained from DL and HC groups.

Platform	Metabolites	Relative Abundance in DL monkeys		Relative Abundance in HC monkeys		P value	DL/CON
GC/LC	Name	Mean	Std	Mean	Std		UP/DOWM
GC	cyanoalanine	-3.069741591	2.847110897	0.130130491	0.363860466	0.039872	Down
GC	conduritol-beta-expoxide	4.349879667	0.871098044	5.848714217	1.24148279	0.036013	Down
GC	2-hydroxyglutaric acid	2.0070788	0.227192808	2.572274519	0.296557942	0.004069	Down
GC	beta-alanine	1.228858863	0.286295329	0.602701628	0.559760134	0.03488	Up
GC	1-monostearin	3.716016023	0.209283788	2.992628298	0.600452191	0.019232	Up
GC	octadecanol	4.669274033	0.481586622	3.553431277	0.870105674	0.025729	Up
GC	sarcosine	5.37536713	2.2223188	2.166330419	2.006801966	0.025373	Up
GC	glycerol-1-phosphate	4.814278427	2.689406593	1.463080118	1.954487996	0.033156	Up
GC	3-arylcarbonyl-alanine	4.162501317	2.378973928	0.191288551	2.812636172	0.024709	Up
GC	galactose-6-phosphate	6.184364798	0.517663825	0.747968361	0.99872515	3.32E-07	Up
LC	(-)-11-hydroxy-9,10-dihydrojasmonic acid 11-beta-D-glucoside	4.219022676	0.724608021	3.057190179	1.03637993	0.04814	Up
LC	(6R)-25-hydroxyvitamin D3 6,19-sulfur dioxide adduct / (6R)-25-hydroxycholecalciferol 6,19-sulfur dioxide adduct	10.95120954	0.541309899	10.22392392	0.531125097	0.040702	Up
LC	(6S)-dehydrovomifoliol	7.697762431	0.062326168	7.590064456	0.044496121	0.00628	Up
LC	(E)-4-Nitrostilbene	1.333652658	0.206639934	1.619208171	0.150133874	0.020887	Down
LC	12,13-DiHODE	2.409582614	1.562011647	0.257329829	0.72234976	0.011975	Up
LC	13-chloro-docosane-1,14-disulfate	5.369651981	1.202742251	3.830814061	0.985691327	0.035819	Up
LC	15-deoxy-delta-12,14-PGJ2-d4	4.104111205	1.467344038	2.322733844	0.945508623	0.031463	Up
LC	1alpha,25-Dihydroxyvitamin D3 25-trimethylsilyl ether	3.18722528	1.742326555	0.165406986	1.694604609	0.012348	Up
LC	24,24-difluoro-1alpha-hydroxyvitamin D3 /	6.13732251	0.233802179	6.681593855	0.308512172	0.006288	Down

	24,24-difluoro-1alpha-hydroxycholecalciferol						
LC	26,27-diethyl-1alpha,25-dihydroxy-22-thiavitamin D3 / 26,27-diethyl-1alpha,25-dihydroxy-22-thiacholecalciferol	4.24748918	1.51695535	1.671134777	1.211035799	0.008703	Up
LC	2-hydroxy-eicosanoic acid	6.905084599	0.963141007	5.581534084	0.328696867	0.018313	Up
LC	2-oxo-heneicosanoic acid	6.591858699	0.730413926	7.391788821	0.239502836	0.02891	Down
LC	3alpha,7beta,12alpha-Trihydroxy-6-oxo-5alpha-cholan-24-oic Acid	6.068329723	0.693002979	5.061231305	0.799632299	0.041955	Up
LC	3'-Deoxydryopteric acid	5.598663335	0.372146178	4.763743868	0.632205037	0.019193	Up
LC	3E,5E-tridecadienoic acid	5.227284365	0.087678174	5.049726723	0.050617949	0.001571	Up
LC	3-O-alpha-L-rhamnopyranosyl-3-hydroxydecanoyl-3-hydroxydecanoic acid	3.865765138	1.854935226	1.364227275	1.600686614	0.031398	Up
LC	4-[5]-ladderane-butanoic acid	5.66722091	0.117264255	5.538652159	0.040606031	0.029475	Up
LC	4'-Hydroxy-4-(4-hydroxystyryl)-5,7-dimethoxyflavan	10.93288342	0.436399272	9.851709764	0.936690003	0.028236	Up
LC	6Z,9Z-Pentacosadiene	2.498158507	0.551675697	3.08384504	0.279506573	0.042791	Down
LC	7-Dehydrocholesterol	5.826753284	0.900022773	7.107797771	0.962498681	0.038529	Down
LC	9,10-DHOME	7.335574515	0.502663081	6.366030474	0.887636309	0.042184	Up
LC	9S,10S,11R-trihydroxy-12Z,15Z-octadecadienoic acid	4.148373944	2.086764639	1.898013376	1.249945546	0.04688	Up
LC	9Z,11E,13-Tetradecatrienal	4.69595241	0.825179524	5.910047598	0.978710872	0.042548	Down
LC	Acetaldehyde	1.415782329	1.301073846	-0.635576542	0.788195259	0.007971	Up
LC	Adenosine triphosphate	8.518493879	0.572560149	9.33571554	0.234240864	0.008932	Down
LC	alhpa-tocopheronic acid	4.120096906	1.546029995	2.488051012	0.853320815	0.047061	Up
LC	C17 Sphinganine-1-phosphate	2.815656	0.660467073	3.521138346	0.387947797	0.047688	Down
LC	Ceramide (d18:1/18:0)	4.527556798	0.647561758	3.680899624	0.606980839	0.041579	Up
LC	Ceramide (d18:1/20:0)	3.614442269	0.616845131	2.677106213	0.48473903	0.015128	Up
LC	DG(14:0/18:3(6Z,9Z,12Z)/0:0)	3.635890869	0.771616892	4.547822234	0.536049118	0.038777	Down
LC	DG(18:2(9Z,12Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	4.686519379	1.379502202	3.099840672	0.717059034	0.031457	Up
LC	Digoxin	5.416674126	1.998536701	2.212605794	1.366610122	0.008845	Up

LC	D-Limonene	0.767782468	0.932865433	1.903921999	0.626525953	0.032736	Down
LC	Dodecanoic acid	3.699259001	0.360421922	3.306331973	0.231774292	0.048502	Up
LC	Estriol 3-sulfate 16-glucuronide	4.2624771	0.699817284	3.442707082	0.445222564	0.036004	Up
LC	farnesyl triphosphate	0.109060533	1.166237027	1.784646586	0.221990547	0.006151	Down
LC	fumagillin	4.859467493	0.129622566	4.563636706	0.194205414	0.011184	Up
LC	Gama-Tocopherol	1.330349072	0.613929459	2.278569339	0.501037515	0.015014	Down
LC	Glepidotin C	12.05640962	0.061417842	11.98624752	0.04535958	0.048106	Up
LC	Heneicosanedioic acid	4.401435658	0.432487564	4.832703334	0.180148565	0.047789	Down
LC	Hippuristanolide	5.52384203	3.429849577	7.210521435	0.144762955	0.024975	Down
LC	Indolelactic acid	1.735393665	0.566514613	3.343476502	1.461021015	0.030718	Down
LC	Kazinol H	6.814089289	0.352143133	7.275954584	0.213687033	0.024497	Down
LC	LysoPC(14:0)	4.276911745	3.467341414	6.228959394	0.3096004	0.037373	Down
LC	LysoPC(18:0)	8.506799964	2.772639332	9.971656069	0.101988139	0.016309	Down
LC	LysoPC(18:1(9Z))	10.96183509	3.721491252	12.64921185	0.040039418	0.037373	Down
LC	LysoPC(18:1(9Z))	12.54694566	2.902816253	14.02895083	0.089661106	0.016309	Down
LC	LysoPC(20:4(5Z,8Z,11Z,14Z))	8.681220293	2.907825622	10.42031183	0.479235026	0.024975	Down
LC	LysoPC(20:4(5Z,8Z,11Z,14Z))	11.14946889	0.284815008	11.80959917	0.565673337	0.028709	Down
LC	methyl 8-[2-(2-formyl-vinyl)-3-hydroxy-5-oxo-cyclopentyl]-octanoate	11.11784573	0.069398021	11.0411855	0.047265314	0.049305	Up
LC	Mevalonic acid	3.439352941	1.788487646	1.123990385	1.698871181	0.044317	Up
LC	MG(18:0/0:0/0:0)[rac]	7.016377528	0.530048051	7.766264715	0.198316114	0.008784	Down
LC	MGDG(16:0/18:2(9Z,12Z))	4.367430218	0.484087832	3.746768602	0.417973544	0.038805	Up
LC	Mutisianthol	2.22139761	0.761814219	3.163613613	0.571549055	0.035856	Down
LC	N-(6-aminohexanoyl)-6-aminohexanoic acid	2.556130218	0.620373758	1.526470358	0.593419535	0.01484	Up
LC	N-methyl arachidonoyl amine	1.162949147	0.201138783	0.796988699	0.348071027	0.049855	Up
LC	Ophionin	2.088920621	0.201492228	2.610287544	0.412006064	0.019301	Down

LC	PA(16:0/0:0)	3.031584893	0.190804557	3.861777651	0.243750869	6.32E-05	Down
LC	PA(17:1(9Z)/22:2(13Z,16Z))	2.568307486	0.294057789	2.953476425	0.146120135	0.016576	Down
LC	PA(18:0/0:0)	1.630664111	0.781123553	2.876939166	0.390430278	0.005767	Down
LC	PA(18:0/0:0)	3.54593137	0.201894865	3.796922365	0.054595896	0.027427	Down
LC	PA(20:1(11Z)/0:0)	2.048681816	0.301030788	2.465749965	0.210692796	0.019439	Down
LC	PA(22:1(11Z)/0:0)	4.66257963	0.354097175	5.083961503	0.158052551	0.023825	Down
LC	PA(P-18:0/0:0)	2.804413888	1.173462446	4.146617908	0.831818777	0.045344	Down
LC	PC(10:0/10:0)	4.905798884	0.189838859	5.099166744	0.083737784	0.045568	Down
LC	PC(14:1(9Z)/24:1(15Z))	4.181542033	0.102464746	4.034237272	0.107645031	0.035578	Up
LC	PC(16:0/3:1(2E))	3.975868837	3.062749834	5.71843867	0.354202507	0.037373	Down
LC	PC(16:0/O-1:0)	9.328539527	0.328661544	9.738837479	0.273512761	0.040608	Down
LC	PC(17:0/0:0)	9.51237883	3.941660191	11.39461644	0.081327869	0.024975	Down
LC	PC(17:1(10Z)/0:0)	9.982782301	0.192283181	10.21466298	0.035801177	0.031083	Down
LC	PC(18:1(9E)/2:0)	10.57858672	2.624350067	11.94529443	0.088184798	0.037373	Down
LC	PC(22:4(7Z,10Z,13Z,16Z)/P-18:0)	11.05590898	2.695568	12.68946475	0.484990888	0.037373	Down
LC	PC(7:0/0:0)	4.512885047	2.640059044	1.671363503	1.6501728	0.04937	Up
LC	PE(12:0/15:1(9Z))	5.381735962	1.176707687	3.920848023	0.580902212	0.021307	Up
LC	PE(18:2(9Z,12Z)/20:5(5Z,8Z,11Z,14Z,17Z))	5.426312295	0.741073976	6.156796064	0.285804714	0.047955	Down
LC	PE(18:2(9Z,12Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	7.537216648	0.472616156	8.40201123	0.6443376	0.024275	Down
LC	PE(18:4(6Z,9Z,12Z,15Z)/22:5(4Z,7Z,10Z,13Z,16Z))	3.699666271	0.880471787	4.875766853	0.809782513	0.036793	Down
LC	PE(20:4(5Z,8Z,11Z,14Z)/0:0)	1.236742202	1.212537104	2.587113449	0.347432959	0.04063	Down
LC	PE(20:4(5Z,8Z,11Z,14Z)/0:0)	3.890172491	0.327272686	4.45513581	0.311557082	0.011991	Down
LC	PE(22:4(7Z,10Z,13Z,16Z)/0:0)	8.669080271	0.295562334	9.342885735	0.56099126	0.026359	Down
LC	PE(O-16:0/21:0)	9.67205635	1.042865526	8.075622916	1.35223403	0.045018	Up
LC	Pelargonidin 3-(6''-malonylglucoside)-5-glucoside	5.103405889	0.215926996	5.679795888	0.330033912	0.005013	Down

LC	**Pelargonidin 3-sambubioside-5-glucoside**	**4.249210614**	**0.532275054**	**4.841017484**	**0.373106594**	**0.049832**	**Down**
LC	**PI(18:2(9Z,12Z)/0:0)**	**4.884709762**	**0.399491531**	**5.432173611**	**0.301321597**	**0.023095**	**Down**
LC	**Prostaglandin E2**	**8.855826169**	**0.055409626**	**8.777439562**	**0.053913854**	**0.032344**	**Up**
LC	**Protorifamycin I**	**6.081389595**	**0.280802175**	**6.47056095**	**0.080009177**	**0.017972**	**Down**
LC	**PS(10:0/10:0)**	**3.133215461**	**3.446281844**	**-0.891346601**	**2.650415114**	**0.04677**	**Up**
LC	**Sphingosine-1-phosphocholine**	**5.275863386**	**1.157139922**	**4.08216185**	**0.584976456**	**0.047764**	**Up**
LC	**undecaprenyl phosphate**	**4.304941907**	**0.793637054**	**5.348946972**	**0.553609193**	**0.024616**	**Down**
LC	**Xestoaminol C**	**10.63753523**	**0.11813885**	**10.4590454**	**0.091594255**	**0.015177**	**Up**

Sup Table 4e. Metabolomic analysis of liver samples obtained from DL and HC groups.

Platform	Metabolites	Relative Abundance in DL monkeys		Relative Abundance in HC monkeys		P value	DL/CON
GC/LC	Name	Mean	Std	Mean	Std		UP/DOWM
GC	Creatinine	4.755754777	0.833425	3.356834589	0.915646	0.01987	Up
LC	(+)-Hirusten-12-oic acid	3.145669091	0.247748067	3.611543031	0.373305999	0.029012	Down
LC	(+)-Myristinin A	3.874071679	0.215202398	4.123213206	0.161000324	0.046518	Down
LC	(21-Methyl-8Z-pentatriacontene	6.18448845	0.151436129	6.472488974	0.245830657	0.034653	Down
LC	11alpha-(4-dimethylaminophenyl)-1alpha,25-dihydroxyvitamin D3 /11alpha-(4-dimethylaminophenyl)-1alpha,25-dihydroxycholecalciferol	5.367093613	0.259775291	5.665547949	0.19572622	0.048373	Down
LC	1-Heptene	10.96319316	0.159835602	11.22713709	0.217951314	0.037824	Down
LC	2,5-dimethyl-2E-tridecenoic acid	5.617018677	0.172033314	5.826805876	0.143781437	0.044864	Down
LC	21-hydroxy-heneicosanoic acid	4.973173956	0.69992136	3.419582949	0.981228895	0.010204	Up
LC	2-amino-14,16-dimethyloctadecan-3-ol	4.60185269	0.313779946	4.197152016	0.293017808	0.043581	Up
LC	2E,4E,6E-Nonatrienal	5.394928788	0.203489176	5.790657976	0.287133413	0.020326	Down
LC	2E-Hexene	6.649429739	0.168725925	6.924661061	0.239850457	0.044332	Down
LC	2-hydroxy behenic	7.901366728	1.495168293	5.817634926	1.355494277	0.029917	Up
LC	2-oxo-tricosanoic acid	3.682304887	0.536976633	2.881307717	0.664106524	0.044453	Up
LC	3,5-Di-O-methyl-8-prenylafzelechin-4beta-ol	-0.071888031	0.734524271	0.742496569	0.39147743	0.044858	Down
LC	3,5-Di-O-methyl-8-prenylafzelechin-4beta-ol	10.41359902	0.229479773	10.84391833	0.237334897	0.009608	Down
LC	3,7,11,15-Tetramethyl-6,10,14-hexadecatrien-1-ol	4.0918842	0.16622028	4.326940414	0.180497597	0.040885	Down
LC	3alpha,12alpha-Dihydroxy-6-oxo-5beta-chol-7-en-24-oic Acid	3.889238211	0.217980893	4.186602743	0.226322167	0.042915	Down
LC	4,2',4'-Trihydroxy-3-methoxydihydrochalcone	4.547088824	0.143137862	4.720210923	0.124827902	0.049605	Down
LC	4-Heptanone	5.855591056	0.155739878	6.103350761	0.183507712	0.030311	Down

LC	6-[3]-ladderane-1-hexanol	5.913590415	0.605592777	6.872925113	0.651196204	0.024629	Down
LC	Anastatin A	3.047717242	1.289298524	0.995124475	1.353945125	0.02273	Up
LC	Betaine	7.76632788	0.186456663	8.149879427	0.301042195	0.024181	Down
LC	beta-vinyl acrylic acid	4.412649106	0.145465071	4.588189549	0.119960998	0.045747	Down
LC	Citrulline	4.401081236	0.20259489	4.756973918	0.228212424	0.017054	Down
LC	Cucurbitacin H	4.556205862	0.163275538	4.838100543	0.20335133	0.024408	Down
LC	DG(14:1(9Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	3.91603217	0.265895255	4.38370013	0.436357564	0.048852	Down
LC	DG(20:4(5Z,8Z,11Z,14Z)/22:5(4Z,7Z,10Z,13Z,16Z)/0:0)	2.906184859	0.64449171	3.626208156	0.339320363	0.035972	Down
LC	DHA (d5)	1.931666913	0.751009419	3.12604093	0.689202066	0.016664	Down
LC	dimethylallyl-diphosphate	3.157651533	0.252517072	3.448374068	0.150075527	0.0358	Down
LC	Docosanedioic acid	7.990474259	0.198848924	8.246861331	0.19260771	0.046686	Down
LC	Epinephrine sulfate	2.466992259	0.314418462	1.996251311	0.390049536	0.044137	Up
LC	Gibberellin A53	5.727752773	1.114453308	4.09127489	1.024943833	0.024419	Up
LC	m-Cresol	5.964669464	0.158720521	6.194577822	0.15250208	0.028446	Down
LC	N-methyl arachidonoyl amine	3.465922496	0.392006664	4.001135353	0.408996627	0.043204	Down
LC	N-palmitoyl methionine	5.034008188	0.758904456	3.105101567	1.564845889	0.021682	Up
LC	PC(16:0/16:0)	12.63443702	0.243539437	12.9445153	0.212982486	0.040805	Down
LC	PC(16:0/5:0)	3.277841303	0.951325006	1.736384522	1.262688169	0.038069	Up
LC	PC(18:0/22:5(7Z,10Z,13Z,16Z,19Z))	8.435934254	0.264356605	8.882805927	0.292572109	0.019585	Down
LC	PC(18:0/22:5(7Z,10Z,13Z,16Z,19Z))	7.108979363	0.199419454	7.421156722	0.196191515	0.021069	Down
LC	PC(18:2(9Z,12Z)/20:5(5Z,8Z,11Z,14Z,17Z))	12.07677765	0.588313787	12.81956011	0.487018906	0.038463	Down
LC	PE(14:0/P-18:0)	8.20896012	0.356204695	7.438318846	0.533638801	0.014732	Up
LC	PE(20:3(8Z,11Z,14Z)/0:0)	7.721269018	1.080688524	6.499011637	0.733402296	0.044835	Up
LC	PE(22:5(4Z,7Z,10Z,13Z,16Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	7.062655428	0.414102114	7.682370107	0.431001171	0.029377	Down
LC	PG(14:0/0:0)	5.712565604	0.231999028	6.159345429	0.362568549	0.029239	Down

LC	**PG(16:0/22:4(7Z,10Z,13Z,16Z))**	**9.488188565**	**0.42659856**	**10.20152281**	**0.515886048**	**0.026033**	**Down**
LC	**PG(18:2(9Z,12Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))**	**12.47773589**	**0.369088063**	**13.01936949**	**0.370279788**	**0.029481**	**Down**
LC	**PI(16:0/20:2(11Z,14Z))**	**12.67783545**	**0.313886659**	**13.17114968**	**0.248420663**	**0.012925**	**Down**
LC	**PI(16:0/22:5(4Z,7Z,10Z,13Z,16Z))**	**12.23839045**	**0.447113104**	**12.86950039**	**0.290407702**	**0.015845**	**Down**
LC	**PI(18:0/0:0)**	**13.15006488**	**0.539527006**	**13.77722842**	**0.350429703**	**0.038096**	**Down**
LC	**PI(20:3(8Z,11Z,14Z)/0:0)**	**8.06085466**	**0.755975406**	**8.82473686**	**0.183144833**	**0.036965**	**Down**
LC	**PI(P-18:0/19:1(9Z))**	**5.261229461**	**0.673142137**	**6.125532778**	**0.51925707**	**0.031975**	**Down**
LC	**Pregnenolone**	**2.474517395**	**1.036853212**	**3.880034569**	**0.874846853**	**0.029475**	**Down**
LC	**Pregnenolone sulfate**	**-0.639756248**	**1.451981759**	**2.192264843**	**0.986614172**	**0.002723**	**Down**
LC	**PS(O-16:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))**	**3.431450117**	**0.950210203**	**0.446313342**	**2.705602699**	**0.042179**	**Up**
LC	**Pyridoxal**	**3.261290071**	**0.238822453**	**3.617180405**	**0.202462544**	**0.019307**	**Down**
LC	**Scillirosidin**	**6.133644109**	**0.2428385**	**6.569080529**	**0.384968481**	**0.041105**	**Down**
LC	**SM(d16:1/17:0)**	**11.18199074**	**0.443745379**	**11.81024494**	**0.410378649**	**0.029058**	**Down**
LC	**SM(d16:1/18:1)**	**11.84003806**	**0.501650353**	**12.56888021**	**0.201113169**	**0.007969**	**Down**
LC	**SM(d18:1/18:1(9Z))**	**9.324755483**	**0.573817983**	**10.14542294**	**0.408428191**	**0.01713**	**Down**
LC	**Stoloniferone F**	**3.992290003**	**0.393766056**	**4.645946466**	**0.537188659**	**0.037067**	**Down**
LC	**terpentecin**	**1.535482102**	**1.70562017**	**-0.462535661**	**0.952593284**	**0.031169**	**Up**

Sup Table 4f. Metabolomic analysis of prefrontal cortex samples obtained from DL and HC groups.

Platform	Metabolites	Relative Abundance in DL monkeys		Relative Abundance in HC monkeys		P value	DL/CON
GC/LC	Name	Mean	Std	Mean	Std		UP/DOWM
GC	Malate	-5.007463818	1.229998277	0.041624472	2.076560859	0.000448	Down
GC	Isochlorogenic Acid	-3.411974647	1.110231753	1.367523249	4.122428895	0.035321	Down
GC	2,5-Dihydroxypyrazine	-1.94018603	1.649764629	2.481972932	2.374589158	0.003807	Down
GC	Palatinitol	1.017668707	2.623591436	4.398946296	1.04106074	0.023668	Down
GC	Glucose	-3.992870252	0.74534809	-0.892800547	2.695194967	0.036309	Down
GC	Adenosine	-4.208078062	0.747952969	-2.157627066	1.62139492	0.025903	Down
GC	Butylamine	-2.145198423	0.428957316	-2.910533879	0.360499812	0.007419	Up
GC	N-Acetyl-5-Hydroxytryptamine	-3.112612162	0.517747579	-3.898072359	0.375296878	0.013146	Up
GC	Oxoproline	-1.359486827	0.293851924	-2.393950403	0.559595768	0.002482	Up
GC	Conduritol-Beta-Expoxide	1.974947252	0.859596622	0.819145182	0.910095104	0.047247	Up
GC	Galactinol	-0.011227594	0.631593906	-1.97396537	1.859859788	0.049042	Up
LC	1'',2''-Dihydro-8-hydroxyisopentanyl-3'-methoxy-4'-O-methylalpinumisoflavone	2.174240714	1.034404428	0.548076134	1.40314086	0.045397	Up
LC	10-oxo-docosanoic acid	2.308665654	0.630580118	3.18625939	0.387930199	0.015737	Down
LC	12beta-hydroxy-24-norcholesta-1,4,22E-trien-3-one	2.632802476	0.694720551	1.836559764	0.45736033	0.040995	Up
LC	14-methyl-8-hexadecen-1-ol	1.736947307	1.216041922	3.230107974	0.620569587	0.023132	Down
LC	14-methyl-8-hexadecen-1-ol	8.486470216	1.056630823	9.647380989	0.272367006	0.042566	Down
LC	1alpha,24-dihydroxy-25,26,27-trinorvitamin D3 / 1alpha,24-dihydroxy-25,26,27-trinorcholecalciferol	2.71405954	0.45241845	1.615398912	1.025634459	0.037271	Up
LC	27-nor-22R-hydroxy-5alpha-cholestan-3,6-dione	8.104317484	0.604810993	7.407056682	0.202256033	0.036018	Up
LC	2-chlorohexadecanol	4.910831381	0.530111862	5.861975979	0.612444414	0.01649	Down

LC	2-fluoro-hexadecanoic acid	-1.29317205	0.466786646	0.408816427	1.808663918	0.049683	Down
LC	3,4-Didehydro-beta-carotene	1.242767449	0.981840003	2.485417761	0.530291767	0.021276	Down
LC	3,7,11-Trimethyldodeca-2E,4E-diene	6.805511842	0.535737599	5.957178377	0.712663293	0.042001	Up
LC	3-O-alpha-L-rhamnopyranosyl-3-hydroxydecanoic acid	3.492395611	0.88271149	4.542891093	0.356895427	0.022216	Down
LC	3Z,6Z,9Z-Pentacosatriene	0.632721645	0.777576316	-0.520635565	0.963112982	0.045604	Up
LC	4,7,10,13-Docosatetraynoic acid	-0.329290245	1.224665291	3.351931145	0.954793446	0.000171	Down
LC	5,8,11-dodecatriynoic acid	4.187546361	0.267137452	3.849939714	0.176891872	0.027366	Up
LC	9-hexadecen-1-ol	4.102776942	0.181711615	3.833174376	0.160767609	0.021491	Up
LC	9-pentadecen-1-ol	2.996105678	0.659853971	3.848603099	0.548621304	0.035244	Down
LC	Anandamide (20:2, n-6)	9.458130751	0.52445027	8.703068882	0.594747405	0.041875	Up
LC	Axillarin 7-sulfate	1.476646609	2.21033383	3.798927577	1.187711364	0.046809	Down
LC	CE(20:0)	1.527406973	0.768873356	2.793706578	0.221593711	0.003077	Down
LC	CerP(d18:1/18:0)	6.954450753	0.228340717	7.210237543	0.121892112	0.036024	Down
LC	Eicosenoic acid	4.378525147	0.652983208	1.101458408	1.258386414	0.000209	Up
LC	Glutathione	7.516087663	1.534924918	9.660844835	1.57594073	0.038083	Down
LC	Grandiflorone	0.644886703	0.885578087	2.074460656	0.593261151	0.008217	Down
LC	Isorhamnetin 3-glucuronide-7-sulfate	2.413072669	1.358213656	4.335999544	1.485283566	0.04132	Down
LC	LysoPC(15:0)	1.402488893	0.442612552	2.293519337	0.325595149	0.002634	Down
LC	Neomethymycin	2.370671655	0.066213877	2.107019159	0.240003178	0.026768	Up
LC	Norepinephrine	3.586172146	0.233876596	3.936338805	0.204214038	0.020042	Down
LC	N-stearoyl GABA	3.440052313	0.618067763	2.285517164	0.842600914	0.022074	Up
LC	PA(22:4(7Z,10Z,13Z,16Z)/0:0)	6.072664081	0.487160458	3.456764961	1.263874862	0.000803	Up
LC	PG(20:5(5Z,8Z,11Z,14Z,17Z)/0:0)	0.687705705	1.612449015	2.913940469	0.893413977	0.014333	Down
LC	PGE2alpha dimethyl amine	6.056990698	0.562813805	5.179931873	0.696841073	0.037417	Up
LC	PI(20:1(11Z)/22:2(13Z,16Z))	2.082353447	0.349955578	3.105796053	0.485566937	0.001863	Down

LC	**plastoquinol-1**	**1.847475606**	**1.563397395**	**3.351713131**	**0.39540502**	**0.045409**	**Down**
LC	**PS(12:0/0:0)**	**2.190248463**	**0.615753478**	**2.942671282**	**0.381839**	**0.029174**	**Down**
LC	**PS(O-20:0/0:0)**	**1.514253997**	**0.54426861**	**2.501299106**	**0.520270603**	**0.009314**	**Down**
LC	**Retinoic acid**	**4.593947143**	**0.589538533**	**6.632775116**	**1.920761397**	**0.047885**	**Down**

Sup Table 4g. Metabolomic analysis of amygdala samples obtained from DL and HC groups.

Platform	Metabolites	Relative Abundance in DL monkeys		Relative Abundance in HC monkeys		P value	DL/CON
GC/LC	Name	Mean	Std	Mean	Std		UP/DOWM
GC	Phosphoenolpyruvate	-2.425821229	2.658865351	1.212029318	0.977342959	0.018564	Down
GC	Conduritol-Beta-Expoxide	2.37685435	0.832304851	1.183636911	0.719013694	0.024007	Up
GC	Lactobionic Acid	-2.947803664	2.283554624	-5.396690466	1.101303303	0.048887	Up
GC	Galactose	0.301726949	2.797944037	-3.795353803	0.917833782	0.014118	Up
LC	13E,15E,18Z,20Z-pentacosatetraen-11-ynyl acetate	2.404954503	0.187870386	2.700052355	0.180483489	0.019631	Down
LC	14-methyl-8-hexadecen-1-ol	3.023644993	1.146065872	4.391683691	0.703628286	0.031893	Down
LC	3-Buten-2-one	1.634224191	0.116801143	2.060346151	0.450916174	0.048934	Down
LC	3-Sulfinoalanine	4.39083403	0.065735785	4.123088034	0.248468408	0.045434	Up
LC	4,8-Dimethyl-4E,8E-decadien-10-olide	2.097702333	0.698407873	3.104183145	0.45706808	0.014444	Down
LC	7,4'-Dihydroxy-8-methylflavan	5.362011013	0.164085546	5.105234583	0.101986997	0.008639	Up
LC	9-pentadecen-1-ol	3.719426917	0.853032511	4.9294953	0.510539135	0.013772	Down
LC	Acetylcysteine	2.317600883	0.782730898	0.950279231	1.186078698	0.040169	Up
LC	Arachidonic acid	5.807353839	0.104817335	6.080420407	0.15719726	0.005355	Down
LC	Bismuth	1.687267394	0.489230093	2.924674499	0.598727291	0.002866	Down
LC	Briantheine W	-0.105903736	1.294343062	1.165189797	0.504383167	0.048894	Down
LC	Butyl 4'-O-butanoyl-6-O-hexadecanoyl-neohesperidoside	3.813350991	0.19976881	4.14603259	0.233187459	0.024151	Down
LC	Daidzein	3.016518105	1.162878428	1.39763096	1.100886712	0.032747	Up
LC	DG(22:2(13Z,16Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	10.16229717	0.289425528	10.63040075	0.168016957	0.006479	Down
LC	Dopamine 4-sulfate	3.801763016	0.647443533	1.258617497	2.349114445	0.044739	Up
LC	Gamma-Glutamylglutamine	4.518454298	0.607873126	3.800140225	0.347403922	0.036368	Up

LC	**Glycerophosphocholine**	**2.930720358**	**0.459622038**	**2.335633085**	**0.204714577**	**0.023419**	**Up**
LC	**Heptadecanoic acid**	**8.713461097**	**0.541831246**	**9.716221262**	**0.353175172**	**0.003499**	**Down**
LC	**Heptadecanoic acid**	**7.461367092**	**0.169855153**	**7.200219805**	**0.216452195**	**0.042416**	**Up**
LC	**LysoPC(14:1(9Z))**	**2.077772045**	**0.237660362**	**2.468123576**	**0.269290858**	**0.02381**	**Down**
LC	**Millettocalyxin C**	**4.13108149**	**0.222849033**	**4.548895028**	**0.242921192**	**0.011164**	**Down**
LC	**Nicotinic acid**	**6.368340111**	**0.201122221**	**6.664275765**	**0.169522041**	**0.020273**	**Down**
LC	**Norgestrel**	**2.129919646**	**0.390663076**	**2.698603555**	**0.467483667**	**0.045284**	**Down**
LC	**PC(20:1(11Z)/P-18:1(11Z))**	**4.546941678**	**0.211077319**	**4.83442445**	**0.213877297**	**0.041099**	**Down**
LC	**PC(O-10:1(9E)/2:0)**	**7.959293159**	**0.088069182**	**8.148286778**	**0.157814553**	**0.028298**	**Down**
LC	**PE(14:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))**	**3.584022363**	**0.954132886**	**1.649014741**	**1.420768914**	**0.019804**	**Up**
LC	**PE(20:4(5Z,8Z,11Z,14Z)/P-16:0)**	**9.598326933**	**0.372848632**	**10.01299292**	**0.145919726**	**0.029522**	**Down**
LC	**PG(22:4(7Z,10Z,13Z,16Z)/0:0)**	**4.285487604**	**0.652906464**	**2.183019355**	**2.191262426**	**0.047986**	**Up**
LC	**PI(O-18:0/0:0)**	**1.97395873**	**0.377833536**	**2.479800171**	**0.297805009**	**0.027628**	**Down**
LC	**Pilosanol A**	**5.571490815**	**0.363018525**	**6.008354628**	**0.257098968**	**0.036962**	**Down**
LC	**Pristanic acid**	**7.624941282**	**0.610684846**	**8.621285719**	**0.417056124**	**0.008011**	**Down**
LC	**Pristanic acid**	**5.474680665**	**0.504935742**	**4.864983248**	**0.430295685**	**0.048085**	**Up**

Sup Table 5a. Metabolite count in metabolomic WGCNA modules.

Module	n . Metabolites
Black	25
Blue	306
Brown	62
Green	33
Grey	1
Pink	24
Red	32
Yellow	33

Sup Table 5b. Detailed information of 4 metabolic modules.

Module	Location	Metabolite	Platform	Database ID
black	amygdala	Heptadecanoic acid	LC	HMDB02259
black	intestine	Uracil	GC	HMDB0000300
black	intestine	Oleic acid	LC	HMDB00207
black	intestine	Uridine 5'-monophosphate	LC	HMDB00288
black	intestine	LysoPC(20:0)	LC	HMDB10390
black	intestine	N-linolenoyl-glutamine	LC	LMFA00000004
black	intestine	13,14-dihydroxy-docosanoic acid	LC	LMFA01050211
black	intestine	2-aminomuconic acid semialdehyde	LC	LMFA01060191
black	intestine	diamino-pimelic acid	LC	LMFA01170102
black	intestine	15-HETE-DA	LC	LMFA08020151
black	intestine	PC(18:0/2:0)	LC	LMGP01010779
black	intestine	PC(O-12:0/O-2:0)	LC	LMGP01040017
black	intestine	PC(O-16:0/O-2:0)	LC	LMGP01040041
black	intestine	PC(O-18:0/O-2:1(1E))	LC	LMGP01040056
black	intestine	PC(17:1(10Z)/0:0)	LC	LMGP01050002
black	intestine	PC(O-17:0/0:0)	LC	LMGP01060013
black	intestine	PE(O-18:0/O-18:0)	LC	LMGP02040005
black	intestine	PE(O-20:0/0:0)	LC	LMGP02060005
black	intestine	PS(O-18:0/0:0)	LC	LMGP03060002
black	intestine	PA(18:1(9Z)/0:0)	LC	LMGP10050008
black	intestine	Malvidin 3-glucoside-5-(6''-malonylglucoside)	LC	LMPK12010389

black	intestine	makisterone B	LC	LMST01031017
black	intestine	Minabeolide-1	LC	LMST01160002
black	feces	fumagillin	LC	LMPR0103060003
black	liver	2-oxo-tricosanoic acid	LC	LMFA01060144
blue	amygdala	Galactose	GC	HMDB0000143
blue	amygdala	Glycerophosphocholine	LC	HMDB00086
blue	amygdala	Pristanic acid	LC	HMDB00795
blue	amygdala	Arachidonic acid	LC	HMDB01043
blue	amygdala	Nicotinic acid	LC	HMDB01488
blue	amygdala	Acetylcysteine	LC	HMDB01890
blue	amygdala	Bismuth	LC	HMDB02196
blue	amygdala	Heptadecanoic acid	LC	HMDB02259
blue	amygdala	Dopamine 4-sulfate	LC	HMDB04148
blue	amygdala	DG(22:2(13Z,16Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	LC	HMDB07672
blue	amygdala	PC(20:1(11Z)/P-18:1(11Z))	LC	HMDB08326
blue	amygdala	PE(20:4(5Z,8Z,11Z,14Z)/P-16:0)	LC	HMDB09411
blue	amygdala	LysoPC(14:1(9Z))	LC	HMDB10380
blue	amygdala	Gamma-Glutamylglutamine	LC	HMDB11738
blue	amygdala	14-methyl-8-hexadecen-1-ol	LC	LMFA05000034
blue	amygdala	9-pentadecen-1-ol	LC	LMFA05000050
blue	amygdala	13E,15E,18Z,20Z-pentacosatetraen-11-ynyl acetate	LC	LMFA07010407
blue	amygdala	4,8-Dimethyl-4E,8E-decadien-10-olide	LC	LMFA07040024
blue	amygdala	3-Buten-2-one	LC	LMFA12000018
blue	amygdala	PC(O-10:1(9E)/2:0)	LC	LMGP01020145

blue	amygdala	PI(O-18:0/0:0)	LC	LMGP06060002
blue	amygdala	Pilosanol A	LC	LMPK12020071
blue	amygdala	7,4'-Dihydroxy-8-methylflavan	LC	LMPK12020230
blue	amygdala	Millettocalyxin C	LC	LMPK12110009
blue	amygdala	Butyl 4'-O-butanoyl-6-O-hexadecanoyl-neohesperidoside	LC	LMSL05000005
blue	amygdala	Norgestrel	LC	LMST02030119
blue	amygdala	Conduritol-Beta-Expoxide	GC	NA
blue	intestine	N-Carbamoylaspartate	GC	HMDB0000828
blue	intestine	Carnosine	LC	HMDB00033
blue	intestine	5-Aminovaleric Acid	GC	HMDB0003355
blue	intestine	Adenosine monophosphate	LC	HMDB00045
blue	intestine	Homovanillic acid	LC	HMDB00118
blue	intestine	L-Phenylalanine	LC	HMDB00159
blue	intestine	L-Proline	LC	HMDB00162
blue	intestine	Cholesterol sulfate	LC	HMDB00653
blue	intestine	Leukotriene B4	LC	HMDB01085
blue	intestine	Prostaglandin E2	LC	HMDB01220
blue	intestine	Guanosine monophosphate	LC	HMDB01397
blue	intestine	Allopregnanolone	LC	HMDB01449
blue	intestine	Caffeine	LC	HMDB01847
blue	intestine	Homocysteine thiolactone	LC	HMDB02287
blue	intestine	Coumesterol	LC	HMDB02326
blue	intestine	Menthol	LC	HMDB03352
blue	intestine	9,12,13-TriHOME	LC	HMDB04708

blue	intestine	Dimethyl sulfone	LC	HMDB04983
blue	intestine	Topiramate	LC	HMDB05034
blue	intestine	5-HEPE	LC	HMDB05081
blue	intestine	TG(16:1(9Z)/16:1(9Z)/16:1(9Z))[iso]	LC	HMDB05432
blue	intestine	Tetrahydrocurcumin	LC	HMDB05789
blue	intestine	Iso-Valeraldehyde	LC	HMDB06478
blue	intestine	PE(14:0/15:0)	LC	HMDB08823
blue	intestine	PE(14:0/18:3(9Z,12Z,15Z))	LC	HMDB08831
blue	intestine	PE(14:1(9Z)/24:0)	LC	HMDB08881
blue	intestine	PE(18:1(11Z)/18:1(11Z))	LC	HMDB09025
blue	intestine	LysoPC(22:1(13Z))	LC	HMDB10399
blue	intestine	Cer(d18:0/25:0)	LC	HMDB11770
blue	intestine	PS(18:1(9Z)/20:4(5Z,8Z,11Z,14Z))	LC	HMDB12394
blue	intestine	Hydroxyphthioceranic acid (C31)	LC	LMFA01020320
blue	intestine	26:5(11Z,14Z,17Z,20Z,23Z)	LC	LMFA01030831
blue	intestine	24:3(15Z,18Z,21Z)	LC	LMFA01030902
blue	intestine	methyl 8-[2-(2-formyl-vinyl)-3-hydroxy-5-oxo-cyclopentyl]-octanoate	LC	LMFA01050151
blue	intestine	2-keto-n-caprylic acid	LC	LMFA01060016
blue	intestine	3-keto-n-caprylic acid	LC	LMFA01060017
blue	intestine	3-hydroxy-suberic acid	LC	LMFA01170093
blue	intestine	13-keto-9Z,11E,15Z-octadecatrienoic acid	LC	LMFA02000028
blue	intestine	PGF2alpha-11-acetate	LC	LMFA03010096
blue	intestine	PGF2alpha-EA(d4)	LC	LMFA03010207
blue	intestine	PGH2-EA	LC	LMFA03010219

blue	intestine	Resolvin D1	LC	LMFA04000006
blue	intestine	13-tetradecen-2,4-diyn-1-ol	LC	LMFA05000016
blue	intestine	14-methyl-8-hexadecen-1-ol	LC	LMFA05000034
blue	intestine	2,6,8,12-Tetramethyl-2,4-tridecadien-1-ol	LC	LMFA05000170
blue	intestine	12,13-Dimethyl-5,14-dioxabicyclo[9.2.1]-tetradeca-1(13),11-dien-4-one	LC	LMFA07040039
blue	intestine	N,N-(2,2-dihydroxy-ethyl) arachidonoyl amine	LC	LMFA08020028
blue	intestine	N-stearoyl GABA	LC	LMFA08020106
blue	intestine	7-Ethyl-3,11-dimethyl-1,3Z,6E,10-tridecatetraene	LC	LMFA11000124
blue	intestine	3Z,6Z,9Z,12Z,15Z-Tricosapentaene	LC	LMFA11000180
blue	intestine	11-Methylhexacosane	LC	LMFA11000214
blue	intestine	1-Octacosene	LC	LMFA11000324
blue	intestine	TG(12:0/12:0/18:1(9Z))[iso3]	LC	LMGL03012638
blue	intestine	PC(16:0/2:0)	LC	LMGP01010612
blue	intestine	PC(18:1(9Z)/4:0)	LC	LMGP01010916
blue	intestine	PC(O-16:0/O-18:1(9Z))	LC	LMGP01040039
blue	intestine	PC(O-6:0/O-6:0)	LC	LMGP01040078
blue	intestine	PC(19:1(9Z)/0:0)	LC	LMGP01050130
blue	intestine	PC(O-16:0/0:0)	LC	LMGP01060010
blue	intestine	PS(22:1(11Z)/0:0)	LC	LMGP03050023
blue	intestine	PG(20:2(11Z,14Z)/22:4(7Z,10Z,13Z,16Z))	LC	LMGP04010587
blue	intestine	PG(22:4(7Z,10Z,13Z,16Z)/0:0)	LC	LMGP04050017
blue	intestine	PI(20:4(5Z,8Z,11Z,14Z)/16:1(9Z))	LC	LMGP06010594
blue	intestine	PI(O-18:0/0:0)	LC	LMGP06060002
blue	intestine	PA(O-16:0/14:0)	LC	LMGP10020004

blue	intestine	PA(P-16:0/15:1(9Z))	LC	LMGP10030006
blue	intestine	5-Carboxypyranocyanidin 3-O-beta-glucopyranoside	LC	LMPK12010432
blue	intestine	Dehydrodolineone	LC	LMPK12060060
blue	intestine	5,7,3',5'-Tetrahydroxy-3,6,8,4'-tetramethoxyflavone	LC	LMPK12113358
blue	intestine	Thonningianin B	LC	LMPK12120466
blue	intestine	5,7,4'-Trihydroxyflavanone 7-sulfate	LC	LMPK12140327
blue	intestine	3'-O-methylbatatasin III	LC	LMPK13090040
blue	intestine	Chamazulene	LC	LMPR0103410002
blue	intestine	8beta-Hydroxy-3-longipinen-5-one	LC	LMPR0103490002
blue	intestine	3S-squalene-2,3-epoxide	LC	LMPR0106010010
blue	intestine	Prosafrinine	LC	LMSP01080051
blue	intestine	GlcCer(d16:1/23:0)	LC	LMSP0501AA31
blue	intestine	3beta-Hydroxy-5alpha,6alpha-epoxy-9-oxo-9,10-seco-5-cholest-7-en-11-al	LC	LMST01010120
blue	intestine	zymosterol intermediate 1c	LC	LMST01010170
blue	intestine	12beta,16beta,20R-trihydroxy-cholest-1,4-dien-3-one	LC	LMST01010339
blue	intestine	(23S)-1alpha-hydroxy-25,27-didehydrovitamin D3 26,23-lactone	LC	LMST03020599
blue	intestine	Hydroxycarbamate	GC	NA
blue	intestine	Digalacturonic Acid	GC	NA
blue	intestine	Fructose-1,6-Bisphosphate	GC	NA
blue	intestine	Mannonic Acid	GC	NA
blue	feces	3-arylcarbonyl-alanine	GC	C03450
blue	feces	sarcosine	GC	HMDB0000271
blue	feces	galactose-6-phosphate	GC	HMDB0000645
blue	feces	Mevalonic acid	LC	HMDB00227

blue	feces	Adenosine triphosphate	LC	HMDB00538
blue	feces	Indolelactic acid	LC	HMDB00671
blue	feces	Acetaldehyde	LC	HMDB00990
blue	feces	Prostaglandin E2	LC	HMDB01220
blue	feces	Digoxin	LC	HMDB01917
blue	feces	D-Limonene	LC	HMDB03375
blue	feces	9,10-DHOME	LC	HMDB04704
blue	feces	Ceramide (d18:1/18:0)	LC	HMDB04950
blue	feces	DG(14:0/18:3(6Z,9Z,12Z)/0:0)	LC	HMDB07017
blue	feces	DG(18:2(9Z,12Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	LC	HMDB07266
blue	feces	PC(14:1(9Z)/24:1(15Z))	LC	HMDB07927
blue	feces	PE(18:2(9Z,12Z)/20:5(5Z,8Z,11Z,14Z,17Z))	LC	HMDB09104
blue	feces	PE(18:2(9Z,12Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	LC	HMDB09111
blue	feces	PE(18:4(6Z,9Z,12Z,15Z)/22:5(4Z,7Z,10Z,13Z,16Z))	LC	HMDB09208
blue	feces	12,13-DiHODE	LC	HMDB10201
blue	feces	Estriol 3-sulfate 16-glucuronide	LC	HMDB10356
blue	feces	LysoPC(20:4(5Z,8Z,11Z,14Z))	LC	HMDB10395
blue	feces	13-chloro-docosane-1,14-disulfate	LC	LMFA00000017
blue	feces	3E,5E-tridecadienoic acid	LC	LMFA01030244
blue	feces	2-hydroxy-eicosanoic acid	LC	LMFA01050073
blue	feces	4-[5]-ladderane-butanoic acid	LC	LMFA01140011
blue	feces	9S,10S,11R-trihydroxy-12Z,15Z-octadecadienoic acid	LC	LMFA02000021
blue	feces	(-)-11-hydroxy-9,10-dihydrojasmonic acid 11-beta-D-glucoside	LC	LMFA02020014
blue	feces	15-deoxy-delta-12,14-PGJ2-d4	LC	LMFA03010177

blue	feces	9Z,11E,13-Tetradecatrienal	LC	LMFA06000182
blue	feces	6Z,9Z-Pentacosadiene	LC	LMFA11000143
blue	feces	MGDG(16:0/18:2(9Z,12Z))	LC	LMGL05010026
blue	feces	PC(10:0/10:0)	LC	LMGP01010380
blue	feces	PC(17:1(10Z)/0:0)	LC	LMGP01050002
blue	feces	PC(16:0/O-1:0)	LC	LMGP01080021
blue	feces	PE(12:0/15:1(9Z))	LC	LMGP02010361
blue	feces	PE(20:4(5Z,8Z,11Z,14Z)/0:0)	LC	LMGP02050009
blue	feces	PI(18:2(9Z,12Z)/0:0)	LC	LMGP06050010
blue	feces	PA(18:0/0:0)	LC	LMGP10050005
blue	feces	PA(16:0/0:0)	LC	LMGP10050006
blue	feces	PA(20:1(11Z)/0:0)	LC	LMGP10050026
blue	feces	PA(22:1(11Z)/0:0)	LC	LMGP10050029
blue	feces	PA(P-18:0/0:0)	LC	LMGP10070002
blue	feces	Protorifamycin I	LC	LMPK05000007
blue	feces	Pelargonidin 3-(6''-malonylglucoside)-5-glucoside	LC	LMPK12010038
blue	feces	Ophionin	LC	LMPK12010354
blue	feces	Kazinol H	LC	LMPK12020242
blue	feces	4'-Hydroxy-4-(4-hydroxystyryl)-5,7-dimethoxyflavan	LC	LMPK12020274
blue	feces	(E)-4-Nitrostilbene	LC	LMPK13090020
blue	feces	(6S)-dehydrovomifoliol	LC	LMPR0103050009
blue	feces	Mutisianthol	LC	LMPR0103360001
blue	feces	undecaprenyl phosphate	LC	LMPR03020001
blue	feces	C17 Sphinganine-1-phosphate	LC	LMSP01040005

blue	feces	Sphingosine-1-phosphocholine	LC	LMSP01060001
blue	feces	24,24-difluoro-1alpha-hydroxyvitamin D3 / 24,24-difluoro-1alpha-hydroxycholecalciferol	LC	LMST03020137
blue	feces	cyanoalanine	GC	NA
blue	feces	glycerol-1-phosphate	GC	NA
blue	feces	2-hydroxyglutaric acid	GC	NA
blue	hippocampus	1-Methylhistidine	LC	HMDB00001
blue	hippocampus	Uridine	GC	HMDB0000296
blue	hippocampus	Mannose-6-Phosphate	GC	HMDB0001078
blue	hippocampus	Dimethylglycine	LC	HMDB00092
blue	hippocampus	L-Glutamic acid	LC	HMDB00148
blue	hippocampus	L-Cystine	LC	HMDB00192
blue	hippocampus	Oleic acid	LC	HMDB00207
blue	hippocampus	Glutamate	GC	HMDB0060475
blue	hippocampus	Myristic acid	LC	HMDB00806
blue	hippocampus	Vanylglycol	LC	HMDB01490
blue	hippocampus	LysoPC(18:1(9Z))	LC	HMDB02815
blue	hippocampus	13S-hydroxyoctadecadienoic acid	LC	HMDB04667
blue	hippocampus	TG(18:2(9Z,12Z)/14:0/18:3(9Z,12Z,15Z))[iso6]	LC	HMDB10471
blue	hippocampus	Cer(d18:0/24:0)	LC	HMDB11768
blue	hippocampus	2E,4E,8Z,10E-dodecatetraenoic acid	LC	LMFA01030240
blue	hippocampus	10E-heptadecen-8-ynoic acid	LC	LMFA01030482
blue	hippocampus	Ambrettolic acid	LC	LMFA01050106
blue	hippocampus	N-ethyl arachidonoyl amine	LC	LMFA08020006
blue	hippocampus	3,5,7-Trimethyl-2E,4E,6E,8E-undecatetraene	LC	LMFA11000055

blue	hippocampus	9,10-Tetracosadiene	LC	LMFA11000536
blue	hippocampus	3-Buten-2-one	LC	LMFA12000018
blue	hippocampus	PC(O-11:1(10E)/2:0)	LC	LMGP01020146
blue	hippocampus	PS(12:0/17:0)	LC	LMGP03010050
blue	hippocampus	PG(18:1(9Z)/0:0)	LC	LMGP04050006
blue	hippocampus	PA(14:0/12:0)	LC	LMGP10010933
blue	hippocampus	PA(P-18:0/20:5(5Z,8Z,11Z,14Z,17Z))	LC	LMGP10030050
blue	hippocampus	Bisdemalonylmonardaein	LC	LMPK12010041
blue	hippocampus	7-Hydroxyflavan	LC	LMPK12020227
blue	hippocampus	CerP(d18:1/18:0)	LC	LMSP02050004
blue	hippocampus	9,11alpha-epoxypregn-4-ene-3,20-dione	LC	LMST02030160
blue	hippocampus	1alpha-hydroxy-26,27-dinorvitamin D3 25-carboxylic acid / 1alpha-hydroxy-26,27-dinorcholecalciferol 25-carboxylic acid	LC	LMST03020025
blue	hippocampus	1alpha,25-dihydroxy-21-nor-20-oxavitamin D3 / 1alpha,25-dihydroxy-21-nor-20-oxacholecalciferol	LC	LMST03020029
blue	liver	Creatinine	GC	HMDB0000562
blue	liver	Betaine	LC	HMDB00043
blue	liver	Pregnenolone	LC	HMDB00253
blue	liver	PC(16:0/16:0)	LC	HMDB00564
blue	liver	Pregnenolone sulfate	LC	HMDB00774
blue	liver	Citrulline	LC	HMDB00904
blue	liver	Pyridoxal	LC	HMDB01545
blue	liver	Epinephrine sulfate	LC	HMDB01876
blue	liver	m-Cresol	LC	HMDB02048
blue	liver	4-Heptanone	LC	HMDB04814
blue	liver	DG(14:1(9Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	LC	HMDB07063

blue	liver	DG(20:4(5Z,8Z,11Z,14Z)/22:5(4Z,7Z,10Z,13Z,16Z)/0:0)	LC	HMDB07525
blue	liver	PC(18:0/22:5(7Z,10Z,13Z,16Z,19Z))	LC	HMDB08056
blue	liver	PC(18:2(9Z,12Z)/20:5(5Z,8Z,11Z,14Z,17Z))	LC	HMDB08149
blue	liver	PE(14:0/P-18:0)	LC	HMDB08851
blue	liver	PE(22:5(4Z,7Z,10Z,13Z,16Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	LC	HMDB09639
blue	liver	PI(16:0/20:2(11Z,14Z))	LC	HMDB09786
blue	liver	PI(16:0/22:5(4Z,7Z,10Z,13Z,16Z))	LC	HMDB09795
blue	liver	PG(16:0/22:4(7Z,10Z,13Z,16Z))	LC	HMDB10581
blue	liver	PG(18:2(9Z,12Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	LC	HMDB10659
blue	liver	2,5-dimethyl-2E-tridecenoic acid	LC	LMFA01020109
blue	liver	beta-vinyl acrylic acid	LC	LMFA01030099
blue	liver	DHA (d5)	LC	LMFA01030762
blue	liver	21-hydroxy-heneicosanoic acid	LC	LMFA01050076
blue	liver	2-hydroxy behenic	LC	LMFA01050077
blue	liver	Docosanedioic acid	LC	LMFA01170037
blue	liver	6-[3]-ladderane-1-hexanol	LC	LMFA05000065
blue	liver	3,7,11,15-Tetramethyl-6,10,14-hexadecatrien-1-ol	LC	LMFA05000210
blue	liver	2E,4E,6E-Nonatrienal	LC	LMFA06000136
blue	liver	N-methyl arachidonoyl amine	LC	LMFA08020007
blue	liver	N-palmitoyl methionine	LC	LMFA08020109
blue	liver	2E-Hexene	LC	LMFA11000035
blue	liver	(21-Methyl-8Z-pentatriacontene	LC	LMFA11000079
blue	liver	1-Heptene	LC	LMFA11000319
blue	liver	PC(16:0/5:0)	LC	LMGP01010672

blue	liver	PS(O-16:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	LC	LMGP03020088
blue	liver	PG(14:0/0:0)	LC	LMGP04050012
blue	liver	PI(P-18:0/19:1(9Z))	LC	LMGP06030046
blue	liver	PI(18:0/0:0)	LC	LMGP06050004
blue	liver	PI(20:3(8Z,11Z,14Z)/0:0)	LC	LMGP06050021
blue	liver	3,5-Di-O-methyl-8-prenylafzelechin-4beta-ol	LC	LMPK12020216
blue	liver	(+)-Myristinin A	LC	LMPK12020229
blue	liver	4,2',4'-Trihydroxy-3-methoxydihydrochalcone	LC	LMPK12120458
blue	liver	Anastatin A	LC	LMPK12140273
blue	liver	dimethylallyl-diphosphate	LC	LMPR01010001
blue	liver	(+)-Hirusten-12-oic acid	LC	LMPR0103730002
blue	liver	2-amino-14,16-dimethyloctadecan-3-ol	LC	LMSP01080031
blue	liver	SM(d18:1/18:1(9Z))	LC	LMSP03010029
blue	liver	SM(d16:1/17:0)	LC	LMSP03010037
blue	liver	SM(d16:1/18:1)	LC	LMSP03010040
blue	liver	Cucurbitacin H	LC	LMST01010109
blue	liver	Stoloniferone F	LC	LMST01031092
blue	liver	Scillirosidin	LC	LMST01130002
blue	liver	11alpha-(4-dimethylaminophenyl)-1alpha,25-dihydroxyvitamin D3 / 11alpha-(4-dimethylaminophenyl)-1alpha,25-dihydroxycholecalciferol	LC	LMST03020538
blue	liver	3alpha,12alpha-Dihydroxy-6-oxo-5beta-chol-7-en-24-oic Acid	LC	LMST04010405
blue	prefrontal cortex	Adenosine	GC	HMDB0000050
blue	prefrontal cortex	Glucose	GC	HMDB0000122

blue	prefrontal cortex	Malate	GC	HMDB0000156
blue	prefrontal cortex	Galactinol	GC	HMDB0005826
blue	prefrontal cortex	Glutathione	LC	HMDB00125
blue	prefrontal cortex	Norepinephrine	LC	HMDB00216
blue	prefrontal cortex	Retinoic acid	LC	HMDB01852
blue	prefrontal cortex	10-oxo-docosanoic acid	LC	LMFA01060139
blue	prefrontal cortex	PGE2alpha dimethyl amine	LC	LMFA03010114
blue	prefrontal cortex	14-methyl-8-hexadecen-1-ol	LC	LMFA05000034
blue	prefrontal cortex	9-pentadecen-1-ol	LC	LMFA05000050
blue	prefrontal cortex	2-chlorohexadecanol	LC	LMFA05000460
blue	prefrontal cortex	N-stearoyl GABA	LC	LMFA08020106
blue	prefrontal cortex	Anandamide (20:2, n-6)	LC	LMFA08040002
blue	prefrontal cortex	3,7,11-Trimethyldodeca-2E,4E-diene	LC	LMFA11000045

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blue	prefrontal cortex	3-O-alpha-L-rhamnopyranosyl-3-hydroxydecanoic acid	LC	LMFA13030003
blue	prefrontal cortex	PG(20:5(5Z,8Z,11Z,14Z,17Z)/0:0)	LC	LMGP04050030
blue	prefrontal cortex	PI(20:1(11Z)/22:2(13Z,16Z))	LC	LMGP06010523
blue	prefrontal cortex	Neomethymycin	LC	LMPK04000036
blue	prefrontal cortex	3,4-Didehydro-beta-carotene	LC	LMPR01070021
blue	prefrontal cortex	plastoquinol-1	LC	LMPR02010037
blue	prefrontal cortex	CerP(d18:1/18:0)	LC	LMSP02050004
blue	prefrontal cortex	27-nor-22R-hydroxy-5alpha-cholestan-3,6-dione	LC	LMST01010334
blue	prefrontal cortex	1alpha,24-dihydroxy-25,26,27-trinorvitamin D3 / 1alpha,24-dihydroxy-25,26,27-trinorcholecalciferol	LC	LMST03020023
blue	prefrontal cortex	2,5-Dihydroxypyrazine	GC	NA
blue	prefrontal cortex	Palatinitol	GC	NA
blue	serum	Beta-Alanine	GC	HMDB0000056
blue	serum	Serine	GC	HMDB0000187

blue	serum	Arabitol	GC	HMDB0000568
blue	serum	PC(16:0/P-18:1(11Z))	LC	HMDB07996
blue	serum	PC(20:5(5Z,8Z,11Z,14Z,17Z)/24:1(15Z))	LC	HMDB08520
blue	serum	18-nonadecynoic acid	LC	LMFA01030503
blue	serum	2-hydroxy-tridecanoic acid	LC	LMFA01050040
blue	serum	PA(17:2(9Z,12Z)/0:0)	LC	LMGP10050022
blue	serum	Prebarbigerone	LC	LMPK12050072
blue	serum	Muxiangrin III	LC	LMPK12111040
blue	serum	Antiarone D	LC	LMPK12120273
blue	serum	5,7,3',4'-Tetrahydroxy-6,5'-di-C-prenylflavanone	LC	LMPK12140405
blue	serum	Adonixanthin 3-glucoside	LC	LMPR01070017
blue	serum	3-demethylubiquinone-9	LC	LMPR02010036
blue	serum	19-norcholestenone	LC	LMST01010313
blue	serum	1,2,4-Benzenetriol	GC	METPA0328
green	amygdala	Phosphoenolpyruvate	GC	HMDB0000263
green	amygdala	3-Sulfinoalanine	LC	HMDB00996
green	intestine	3-Hydroxybutyric Acid	GC	HMDB0000357
green	intestine	methyl 8-[2-(2-formyl-vinyl)-3-hydroxy-5-oxo-cyclopentyl]-octanoate	LC	LMFA01050151
green	intestine	5S,9S-Dimethyloctadecane	LC	LMFA11000027
green	intestine	PC(O-18:0/14:0)	LC	LMGP01020195
green	feces	octadecanol	GC	HMDB0002350
green	feces	Gama-Tocopherol	LC	HMDB01492
green	feces	Ceramide (d18:1/20:0)	LC	HMDB04951
green	feces	Heneicosanedioic acid	LC	LMFA01170036

green	feces	MG(18:0/0:0/0:0)[rac]	LC	LMGL01010003
green	feces	PA(17:1(9Z)/22:2(13Z,16Z))	LC	LMGP10010273
green	feces	3alpha,7beta,12alpha-Trihydroxy-6-oxo-5alpha-cholan-24-oic Acid	LC	LMST04010262
green	hippocampus	Inosine	LC	HMDB00195
green	hippocampus	Eicosenoic acid	LC	HMDB02231
green	hippocampus	DG(18:1(11Z)/22:5(4Z,7Z,10Z,13Z,16Z)/0:0)	LC	HMDB07206
green	hippocampus	PC(15:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	LC	HMDB07958
green	hippocampus	PC(20:4(5Z,8Z,11Z,14Z)/24:1(15Z))	LC	HMDB08454
green	hippocampus	PE(18:3(9Z,12Z,15Z)/20:2(11Z,14Z))	LC	HMDB09165
green	hippocampus	PE(P-18:1(11Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	LC	HMDB11427
green	hippocampus	20-carboxy-LTB4	LC	LMFA03020016
green	hippocampus	1-(6-[5]-ladderane-hexanyl)-2-(8-[3]-ladderane-octanyl)-sn-glycerol	LC	LMGL02030029
green	hippocampus	1-tetradecanyl-2-(8-[3]-ladderane-octanyl)-sn-glycerol	LC	LMGL02030032
green	hippocampus	1-(8-[5]-ladderane-octanoyl)-2-(8-[3]-ladderane-octanyl)-sn-glycerophosphoethanolamine	LC	LMGP02080002
green	hippocampus	PS(17:0/20:3(8Z,11Z,14Z))	LC	LMGP03010241
green	hippocampus	PA(14:0/18:1(9Z))	LC	LMGP10010019
green	prefrontal cortex	N-Acetyl-5-Hydroxytryptamine	GC	HMDB0001238
green	prefrontal cortex	Butylamine	GC	HMDB0031321
green	prefrontal cortex	Isochlorogenic Acid	GC	NA
green	serum	PG(22:4(7Z,10Z,13Z,16Z)/0:0)	LC	LMGP04050017
green	serum	Caloxanthin sulfate	LC	LMPR01070148
green	serum	Fumonisin A1	LC	LMSP01080026

green	serum	1beta,3alpha,7alpha,12alpha-Tetrahydroxy-5beta-cholan-24-oic Acid	LC	LMST04010114
yellow	intestine	Succinic Acid	GC	HMDB0000254
yellow	intestine	Cytosine	LC	HMDB00630
yellow	intestine	Linoleic acid	LC	HMDB00673
yellow	intestine	1-Methylhistamine	LC	HMDB00898
yellow	intestine	D-Sedoheptulose 7-phosphate	LC	HMDB01068
yellow	intestine	LysoPC(18:1(9Z))	LC	HMDB02815
yellow	intestine	LysoPC(16:1(9Z))	LC	HMDB10383
yellow	intestine	LysoPC(22:4(7Z,10Z,13Z,16Z))	LC	HMDB10401
yellow	intestine	Hydroxyphthioceranic acid (C42)	LC	LMFA01020327
yellow	intestine	Tricosanyl palmitoleate	LC	LMFA07010027
yellow	intestine	14-O-(beta-D-glucopyranosyl)-7S,14R-dihydroxy-7,9,13,17-tetramethyl-2E,4E,8E,10E,12E,16E-octadecahexaenoic acid	LC	LMFA13010034
yellow	intestine	PC(O-11:1(10E)/2:0)	LC	LMGP01020146
yellow	intestine	PC(13:0/0:0)	LC	LMGP01050001
yellow	intestine	PC(17:1(10Z)/0:0)	LC	LMGP01050002
yellow	intestine	PC(19:3(10Z,13Z,16Z)/0:0)	LC	LMGP01050003
yellow	intestine	PC(15:1(9Z)/0:0)	LC	LMGP01050125
yellow	intestine	PE(22:4(7Z,10Z,13Z,16Z)/0:0)	LC	LMGP02050014
yellow	intestine	PE(20:1(11Z)/0:0)	LC	LMGP02050020
yellow	intestine	PG(20:4(5Z,8Z,11Z,14Z)/0:0)	LC	LMGP04050010
yellow	intestine	Peonidin	LC	LMPK12010006
yellow	intestine	Viscutin 1	LC	LMPK12020265
yellow	intestine	Dehydrodolineone	LC	LMPK12060060
yellow	intestine	Pongamoside A	LC	LMPK12110010

yellow	intestine	Isorhamnetin 3-(6''-galloylglucoside)	LC	LMPK12110591
yellow	intestine	Naringenin 7-O-(2'',6''-di-O-alpha-rhamnopyranosyl)-beta-glucopyranoside	LC	LMPK12140262
yellow	intestine	2-deoxy-20-hydroxy-5alpha-ecdysone 3-acetate	LC	LMST01010191
yellow	intestine	24-Nor-5beta-chol-22-ene-3alpha,7alpha,12alpha-triol	LC	LMST04060012
yellow	feces	7-Dehydrocholesterol	LC	HMDB00032
yellow	feces	Dodecanoic acid	LC	HMDB00638
yellow	feces	PE(22:4(7Z,10Z,13Z,16Z)/0:0)	LC	LMGP02050014
yellow	feces	Pelargonidin 3-sambubioside-5-glucoside	LC	LMPK12010025
yellow	serum	Pseudouridine	LC	HMDB00767